1838 © *1981 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, *54*, *1838—1840 (1981)* [Vol. 54, No. 6

Syntheses of *N*-Substituted 3,3,4-Triaryl- and 3,3,4,4-Tetraphenyl-2-azetidinones

Kailash Nath MEHROTRA* and Surendra Bahadur SINGH
Department of Chemistry, Banaras Hindu University, Varanasi-221005, India

(Received June 28, 1980)

The reactions of 2-diazo-1,2-diphenylethanone with Schiff's bases Ar–CH=N–R gave new substituted 2-azetidinones together with 1,1′,4,4′-tetraphenyl-2,2′-azinodiethanone. 2-Diazo-1,2-diphenylethanone reacts with *N*-benzhydrylidene-*N*′-phenylurea to give 1-(phenylcarbamoyl)-3,3,4,4-tetraphenyl-2-azetidinone.

The cycloaddition of diphenylketene with anils is known to form 2-azetidinones.[1] Diphenylketene, in these cases, has been generated either thermally by dehydrohalogenation of suitable acid chlorides with tertiary bases[2] or photochemically from diazo ketone.[3] On the other hand, diphenylketene has been known to add on carbon-oxygen double bond in α,β-unsaturated ketones to give β-lactones.[4] We now report the cycloaddition of diphenylketene, generated *in situ* by thermal decomposition of 2-diazo-1,2-diphenylethanone (**1**), with Schiff's bases **2a**—**g** leading to *N*-alkyl-2-azetidinones **3a**—**g** in fair yields. The reaction of diphenylketene with *N*-benzhydrylidene-*N*′-phenylurea (**5**), having three reactive sites (C=N, C=O, and NH), has shown that C=N group is attacked by diphenylketene in preference to either C=O group or NH group. The products, **3a**—**g**, show extraordinary stability amongst β-lactams[5] towards common degradative reagents.

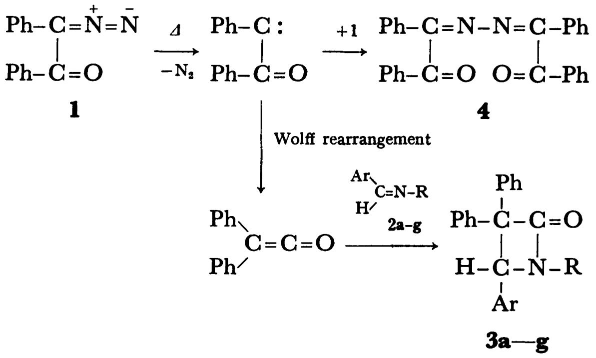
Results and Discussion

An equimolecular mixture of 2-diazo-1,2-diphenylethanone (**1**) and *N*-benzylideneisopropylamine (**2a**: $Ar=C_6H_5$, $R=CH(CH_3)_2$) was heated to reflux in dry benzene for 12 h under stream of nitrogen. The reaction product was separated by fractional crystallization from hexane–ethanol (1 : 1) and vacuum distillation; it consisted of 1,1′,4,4′-tetraphenyl-2,2′-azinodiethanone (**4**, 2%) and 1-isopropyl-3,3,4-triphenyl-2-azetidinone (**3a**, 85%). An authentic sample of product **4** was prepared according to method reported[6] for comparison (IR, NMR, and also melting point). The structural assignment of **3a** was made on the basis of its analytical and spectral data.

Similar treatment of Schiff's bases **2b**—**f** gave 2-azetidinones **3b**—**f**, identified on the basis of their analytical and spectral data, together with ketazine (**4**, 3—5%) in each case.

The racemic *N*-benzylidene-α-methylbenzylamine (**2g**) on similar treatment gave two products, a white crystalline solid **3g** (81%) and a yellow crystalline solid, identified as ketazine **4** (3%). The white crystalline solid, mp 94—95 °C, showed absorption band at 1740 (C=O, β-lactam[2]) cm^{-1} in IR spectrum. The NMR spectrum of product exhibited two doublets at δ 1.47 and 1.92, two quartets at δ 4.32 and 5.01 and one singlet at δ 5.02 which may be due to presence of two enantiomeric forms of product **3g**. This would be expected as the starting Schiff's base **2g** is racemic. The elemental analyses and spectral data agree with assigned structure, (±) 1-(α-methylbenzyl)-3,3,4-triphenyl-2-azetidinone (**3g**), to the product.

The products **3a**—**g** were found to be unaffected on treatment with ordinary alkali or acid, whereas, *N*-aryl-2-azetidinones reported earlier[5] have been known to undergo hydrolysis. The formation of products can be explained as in Scheme 1.

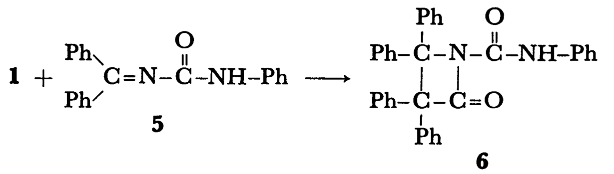


	Ar	R
3a	C_6H_5	$CH(CH_3)_2$
3b	C_6H_5	$CH(C_6H_5)_2$
3c	$p\text{-}CH_3OC_6H_4$	$CH(C_6H_5)_2$
3d	$p\text{-}ClC_6H_4$	$CH(C_6H_5)_2$
3e	$p\text{-}NO_2C_6H_4$	$CH(C_6H_5)_2$
3f	$p\text{-}(CH_3)_2NC_6H_4$	$CH(C_6H_5)_2$
3g	C_6H_5	$CH(CH_3)C_6H_5$

Scheme 1.

Thermal decomposition of **1** may lead to benzoylphenylcarbene which may combine with **1** to form ketazine **4**. The benzoylphenylcarbene has been known to undergo Wolff rearrangement to give diphenylketene[7] which on reaction with C=N bond of Schiff's bases **2a**—**g** may lead to 2-azetidinones **3a**—**g** through the collapse of a possible zwitterionic intermediate. A similar intermediate has been proposed in the reaction of diphenylketene and *N*-benzylideneaniline giving *N*-phenylimidate.[8]

When *N*-benzhydrylidene-*N*′-phenylurea (**5**) was allowed to react with **1**, in an analogous manner, a white crystalline solid (70%) was obtained. The substituted urea **5** contains three possible reactive sites *viz.* C=N, C=O, and NH groups. It is known that interaction of ketene with C=N, C=O, and NH groups leads to the formation of β-lactam,[8] β-lactone[9] (which on decarboxylation gives corresponding olefin) and acetyl derivative[10] of NH group, respectively. The presence of an absorption bands at 1760 cm^{-1}, characteristic of a β-lactam[11] and 1710 (C=O, CONH[11]) cm^{-1}, absence of an absorption band between 1700



and 1600 cm^{-1} in IR spectrum and absence of a signal between δ 6—5 in NMR spectrum strongly support the assigned structure, 1-(phenylcarbamoyl)-3,3,4,4-tetraphenyl-2-azetidinone (**6**), to the product. It appears that diphenylketene adds exclusively on the C=N bond in preference to either C=O or NH bonds. The NH bond in an amide does not react with diphenylketene.[10]

Experimental

Melting points have been determined in capillaries on Büchi melting point apparatus and are uncorrected. The IR spectra were measured in Nujol mull on a Perkin-Elmer 720-spectrophotometer. The NMR spectra were recorded on Varian A-60 MHz spectrometer in CCl_4/$CDCl_3$ with TMS as an internal standard.

Materials. The aldehydes were obtained from BDH, India and 1,[12]-methylbenzylamine,[13] benzhydrylamine,[14] and *N*-benzhydrylidene-*N*′-phenylurea[15] were prepared according to reported methods.

Preparation of Schiff's Bases **2a**—**g**. *General Procedure*: The Schiff's bases **2a**—**g** were obtained by mixing equimolar amount of aldehyde and amine at room temperature. In all the cases, except **2a** where purification was done by vacuum distillation, the products were purified by fractional crystallization from ethanol. Yield: 80—85%.

Preparation of 2-Azetidinones **3a**—**g**. *General Procedure*: A mixture of 0.01 mol of **1** and 0.01 mol of a Schiff's base **2a**—**g** was heated to reflux in 80 ml of dry benzene (free from thiophene) for 12 h under stream of nitrogen. The reaction mixture was kept overnight. The solvent was removed on rotatory evaporator and residual matter was crystallised from ethanol to give 2-azetidinone **3a**—**g**. From the mother liquor 1,1′,4,4′-tetraphenyl-2,2′-azinodiethanone (**4**, 2—5%), mp 202—303 °C (lit,[6] mp 202 °C) [UV (EtOH, nm): 255 and 315; IR (Nujol, cm^{-1}): 1680 (C=O) and 1601 (C=N–N=C); NMR ($CDCl_3$, δ ppm): 8.30—7.20 (m, H, aromatic protons). Found: C, 80.35; H, 5.12; N, 6.83%. Calcd for $C_{28}H_{20}N_2O_2$: C, 80.75; H, 4.84; N, 6.73%] was recovered by evaporation of solvent and recrystallization of residual matter from hexane–ethanol (1 : 1).

1-Isopropyl-3,3,4-triphenyl-2-azetidinone (3a) A yield of 85% obtained, bp 165/0.01 mmHg† (mp 102—103 °C). UV (EtOH, nm): 250, 255, and 260; IR (CCl_4, cm^{-1}): 1740 (C=O, β-lactam); NMR (CCl_4, δ ppm): 7.75—6.90 (m, 15H, aromatic protons); 5.31 (s, 1H, CH, ring); 3.81 (Sept, 1H, CH, isopropyl, J=7 Hz); 1.37 and 1.15 (a pair of doublets, 6H, CH_3, isopropyl, J=7 Hz). Found: C, 84.66; H, 6.72; N, 4.07%. Calcd for $C_{24}H_{23}NO$: C, 84.45; H, 6.74; N, 4.11%.

1-Benzhydryl-3,3,4-triphenyl-2-azetidinone (3b). A yield of 78% was obtained, mp 159—160 °C. UV (EtOH, nm): 250, 255, and 260; IR (Nujol, cm^{-1}): 1742 (C=O, β-lactam); NMR (CCl_4, δ ppm): 7.73—6.87 (m, 25H, aromatic protons); 5.61 (s, 1H, CH, benzhydryl); 5.45 (s, 1H, CH, ring). Found: C, 87.50; H, 5.64; N, 3.24%. Calcd for $C_{34}H_{27}NO$: C, 87.74; H, 5.80; N, 3.01%.

*1-Benzhydryl-3,3-diphenyl-4-(*p*-methoxyphenyl)-2-azetidinone (3c).* A yield of 61% was obtained, mp 129—130 °C. UV (EtOH, nm): 260, 265, and 270; IR (Nujol, cm^{-1}): 1730 (C=O, β-lactam) and 1250 (C–O–C); NMR (CCl_4, δ ppm): 7.70—7.00 (m, 20H, aromatic protons); 6.80 and 6.65 (A_2B_2q, 4H, aromatic protons, J=8 Hz); 5.67 (s, 1H, CH, benzhydryl); 5.27 (s, 1H, CH, ring); 3.67 (s, 3H, CH, OCH_3). Found: C, 84.83; H, 5.74; N, 3.04%. Calcd for $C_{35}H_{29}NO_2$: C, 84.84; H, 5.85; N, 2.83%.

*1-Benzhydryl-3,3-diphenyl-4-(*p*-chlorophenyl)-2-azetidinone (3d).* A yield of 59% was obtained, mp 145—146 °C. UV (EtOH, nm): 250, 260, and 270; IR (Nujol, cm^{-1}): 1735 (C=O, β-lactam); NMR (CCl_4, δ ppm): 7.83—7.03 (m, 20H, aromatic protons); 6.97 and 6.71 (A_2B_2q, 4H, aromatic protons, J=9Hz); 5.65 (s, 1H, CH, benzhydryl); 5.27 (s, 1H, CH, ring). Found: C, 81.79; H, 5.34; N, 2.72%. Calcd for $C_{34}H_{26}NOCl$: C, 81.68; H, 5.20; N, 2.80%.

*1-Benzhydryl-3,3-diphenyl-4-(*p*-nitrophenyl)-2-azetidinone (3e).* A yield of 61% was obtained, mp 206—207 °C. UV (EtOH, nm): 278; IR (Nujol, cm^{-1}): 1735 (C–O, β-lactam), 1520 and 1350 (NO_2); NMR ($CDCl_3$, δ ppm): 8.05—7.00 (m, 24H, aromatic protons); 5.91 (s, 1H, CH, benzhydryl); 5.57 (s, 1H, CH, ring); Found: C, 79.80; H, 5.50; N, 5.45%. Calcd for $C_{34}H_{26}N_2O_3$: C, 80.00; H, 5.09; N, 5.49%.

*1-Benzhydryl-3,3-diphenyl-4-(*p*-dimethylaminophenyl)-2-azetidinone (3f).* A yield of 62% was obtained, mp 150—151 °C. UV (EtOH, nm); 265: IR (Nujol, cm^{-1}): 1730 (C=O, β-lactam); NMR (CCl_4, δ ppm): 7.70—7.00 (m, 20H, aromatic protons): 6.75 and 6.48 (A_2B_2q, 4H, aromatic protons, J=9 Hz); 5.51 (s, 1H, CH, benzhydryl); 5.17 (s, 1H, CH, ring); 2.82 (s, 6H, CH, $-N(CH_3)_2$). Found: C, 85.48; H, 6.54; N, 5.72%. Calcd for $C_{36}H_{32}N_2O$: C, 85.67; H, 6.29; N, 5.51%.

1-(α-Methylbenzyl)-3,3,4-triphenyl-2-azetidinone (3g). A yield of 81% was obtained, mp 94—95 °C. UV (EtOH, nm): 255, 260, and 265; IR (Nujol, cm^{-1}): 1740 (C=O, β-lactam); NMR (CCl_4, δ ppm): 7.67—6.90 (m, 20H, aromatic protons); 5.05 (s, 1H, CH, ring); 5.01 and 4.32 (a pair of quartets, 1H, CH, $CH(CH_3)C_6H_5$, J=7 Hz); 1.92 and 1.47 (a pair of doublets, 3H, CH, $CH(CH_3)C_6H_5$, J=7 Hz). Found: C, 85.90; H, 6.45; N, 3.32%. Calcd for $C_{29}H_{25}NO$: C, 86.35; H, 6.20; N, 3.47%.

Attempted Ring Opening of **3a**—**g**. A mixture containing 0.20 g of **3a**, 15 ml of 85% ethanol and 1 ml of concentrated hydrochloric acid was heated to reflux for 30 h. After the usual work up 0.18 g (90%) of starting material was recovered. Similar treatment of **3a**—**g** with either 40% aqueous alkali (potassium hydroxide or sodium hydroxide) or saturated ethanolic potassium hydroxide solution resulted in recovery of starting material almost quantitatively.

Preparation of 1-(Phenylcarbamoyl)-3,3,4,4-tetraphenyl-2-azetidinone (6). A mixture of 0.01 mol of **1** and 0.01 mol of **5** was heated to reflux in 80 ml of dry benzene (free from thiophene) for 8 h under stream of nitrogen. The reaction mixture was kept overnight. The solvent was removed on rotatory evaporator and residual matter was recrystallized from ethanol to give a white crystalline solid **6** (70%), mp 200—202 °C. UV (EtOH, nm): 235, 250, and 260; IR (Nujol, cm^{-1}): 3310 (NH), 1760 (C=O, β-lactam) and 1710 (C=O, CONH–); NMR ($CDCl_3$, δ ppm): 9.10 (b, 1H, NH, D_2O exchangeable); 7.83—7.05 (m, 25H, aromatic protons). Found: C, 82.77; H, 5.42; N, 6.01%. Calcd for $C_{34}H_{26}N_2O_2$: C, 82.59; H, 5.26; N, 5.68%.

We are thankful to Professor B. M. Shukla for providing the facilities and to C.S.I.R., New Delhi, for grant of a fellowship to SBS.

---

† 1 mmHg≈133.322 Pa.

References

1) A. K. Mukerjee and R. C. Srivastava, *Synthesis*, **1973**, 327, and references cited therein.

2) A. K. Bose and I. Kugajevsky, *Tetrahedron*, **23**, 957 (1967).

3) W. Kirmse and L. Horner, *Chem. Ber.*, **89**, 2759 (1956).

4) H. Staudinger, *Chem. Ber.*, **41**, 1355 (1908).

5) H. T. Clarke, J. R. Johnson, and R. Robinson, "The Chemistry of Penicillin," Princeton University Press (1949), p. 945.

6) T. Curtius and R. Kastner, *J. Prakt. Chem.*, **83**, 215 (1911); *Chem. Abstr.*, **5**, 2649 (1911).

7) V. Franzen, *Justus Liebigs Ann. Chem.*, **614**, 31 (1958).

8) H. B. Kagan and J. L. Luche, *Tetrahedron Lett.*, **1968**, 3093.

9) L. L. Muller and J. Hamer, "1,2-Cycloaddition Reactions," Interscience Publ., New York (1967), p. 139.

10) W. Jugelt and D. Schmidt, *Tetrahedron*, **25**, 969 (1969).

11) G. Wittig and A. Hesse, *Justus Liebigs Ann. Chem.*, **1976**, 500.

12) C. D. Nenitzescu and E. Solomonica, *Org. Synth.*, Coll. Vol. II, 496 (1950).

13) A. W. Ingersoll, *Org. Synth.*, Coll. Vol. II, 503 (1950).

14) A. Michaelis, *Chem. Ber.*, **26**, 2169 (1893).

15) G. E. P. Smith, Jr., and F. W. Bergstrom, *J. Am. Chem. Soc.*, **56**, 2095 (1934).