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A Convenient Synthesis of Azomethine Imines and Their Cycloaddition Reactions with Some Dipolarophiles

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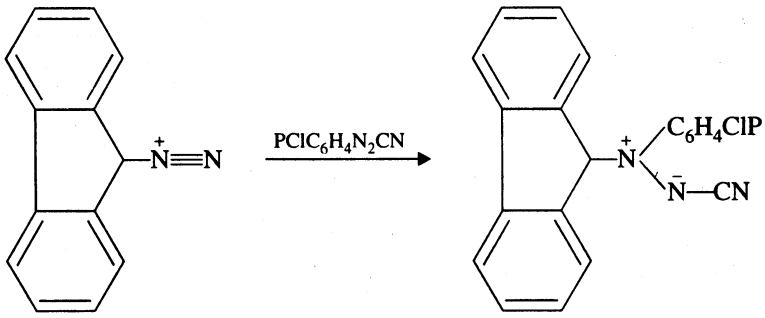
Azomethine imines (**4a–c**) were prepared as 1,3-dipolar structures, from known compounds 5-phenylpyrazolidine-3-one (**3**) and acetone, thiobenzophenone or benzaldehyde. From the reaction of the 1,3-dipoles (**4a–c**) with methyl acrylate, ethyl acrylate, phenylisocyanate, N-phenylmalemide, acetylenedicarboxylate and ethyl propiolate products (**5–12**) were obtained as cyclo-adduct compounds.

Key Words: Synthesis, Azomethine imine, Cycloaddition Dipolarophile 1,3–Dipole

INTRODUCTION

There is a large variety of compounds containing the azomethine imine system[1] of which we shall consider only a few. Huisgen and his group[1] prepared the crystalline N(β)-cyano (azomethine imine) (**2**) from diazocyanide and the diazo-alkane (**1**).

The cycloaddition reaction of azomethine imines with carbon-carbon-nitrogen, carbon-oxygen double bonds such as styrene, acrylic esters norbornene and phenylisocyanate yielded cycloadduct products[1].



RESULTS AND DISCUSSION

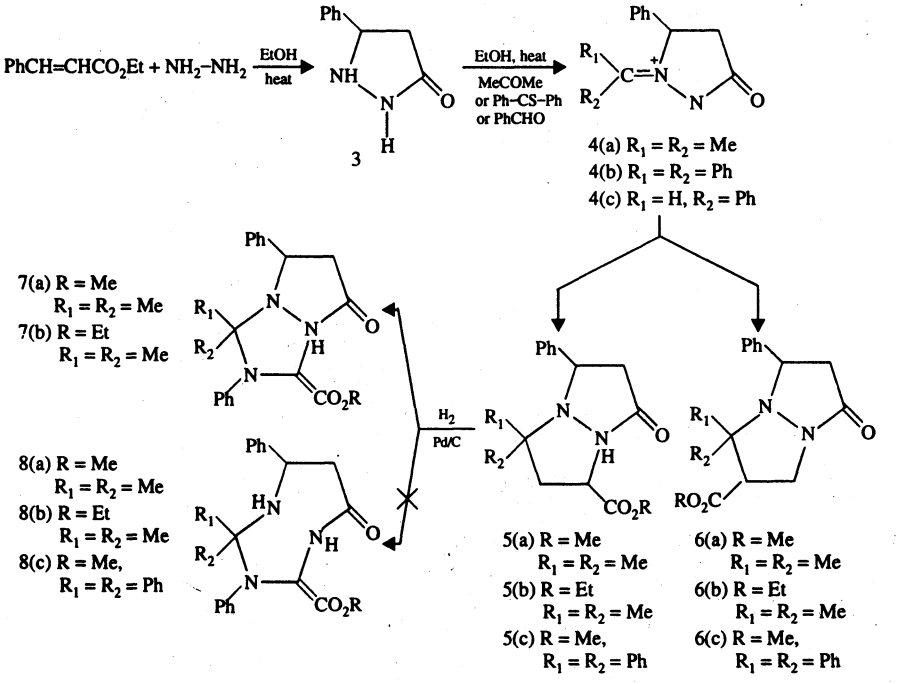
The anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) (**4a**) was reacted as an example with methyl acrylate in dry benzene for 36h and the resulting oil shown by ^{1}H NMR to consist of only two products in the ratio 7 : 1. Recrystallization from ethanol gave the major product (**5a**) as colourless crystals, m.p. 115–117°C (87% yield).

The minor product (**6a**) could only be obtained from the mother liquors by HPLC. Although the spectral data for each of these products confirmed that they were 1,3-dipolar cycloadducts, it did not prove possible even on detailed

examination of their ^1H NMR spectra to unequivocally determine their regiochemistry or whether they were regioisomers or stereoisomers. In view of this difficulty it was decided to resort to chemical transformation to provide more information. Thus the treatment of major product with an excess of 1,5-diazabicyclo[4.3.0]non-5-ene gave after work-up a mixture of two products in a ratio of 7 : 3. The minor product was identified as the starting material by HPLC comparison with authentic sample, while the major component after separation by HPLC afforded another isomer.

When heating a solution of major isomer in dry benzene solution under nitrogen at 80°C overnight, the resulting product was shown by ^1H NMR to consist solely of starting material in quantitative yield.

It was therefore proved that both of the products from the reaction of the dipole **(4)** with methyl acrylate have a common regiochemistry. In order to determine which of the possible regiochemistry is correct, it was decided to treat the major product with reducing agents, since cleavage of N-N bond would result in product **(8)**. A number of methods are known[2-6].



Catalytic hydrogenation indeed form a different product whose spectral data did not, however, fit either of the expected structure (**8**). Instead of the spectral data was consistent with the product having structure (**7**). Thus:

(i) The high resolution mass spectra of the product (**7a**) showed a measured mass of m/z 290.1635 for the molecular ion, which is in good agreement with the calculated mass for $C_{16}H_{22}N_2O_3$ of m/z 290.1631.

(ii) The presence of absorption maximum at 3225 cm^{-1} in the infrared spectrum is in agreement with the observation that most amides possess[7] an N—H group in their infrared spectrum in the region 3400–3100 cm^{-1}.

(iii) The ^1H NMR spectrum of the compound (**7a**) showed in addition of phenyl-methyl, methoxy groups and ABX system, the presence of broad singlet at $\delta = 4.15$ with an integrated intensity of one proton and exchangeable with D_2O arising from N—H proton and multiplet at $\delta = 2.7–3.2$ with an integrated intensity of four protons assignable to the methylene protons on the 2- and 3-positions. The specific irradiation of the signal at $\delta = 4.70$ caused each of the signals at $\delta = 2.25$ and $\delta = 1.72$ to collapse to a doublet ($J = 12$) which is in complete agreement with that expected for the protons H – 5' and 2 × H – 4'.

(iv) The ^{13}C NMR spectrum of the product (**7a**) showed the presence of signals at $\delta = 173.1$ and 172.55 arising from the two carbonyl carbons atom, and three triplet signals at $\delta = 45.4$, 35.2 and 30.9 which were readily assigned (on the basis of off-centre double resonance experiments) to the three methylenes on the C–4, C–2 and C–3 positions respectively.

However, it does prove that both products have single regiochemistry of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazabicyclo[3.3,0]octane-6-one (**5a**) and further evidence by reduction gave methyl-4-methyl-4-(5′-phenylpyrazolidine-3′-one-1-yl)pentanoate (**7a**).

In light of these results obtained from the above reaction, it was decided to check this work with ethyl acrylate. In this case it was also proved that both of the products have a common regiochemistry. From the catalytic hydrogenation of the major product the spectral data are compatible with the structure (**7a**).

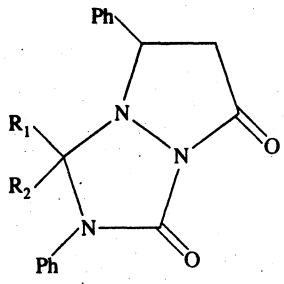
In light of these results we decided to react the novel azomethine imine (**4a**) with other common dipolarophiles. Thus treatment of the compound (**4a**) with phenyl isocyanate gave the expected 2,2-dimethyl-3,8-diphenyl-1,3,5-triazobicyclo[3,3,0]octane-2,4-dione (**9a**) (76% yield). Microanalysis of this product was consistent with the m.f. $C_{19}H_{19}N_3O_2$ required for adduct (**9a**). All spectroscopic data confirmed the structure (**9a**). Furthermore, the reason for the selective formation of one regioisomer is the fact that only one product shown by ^1H NMR is the crude compound and so only one product is isolated.

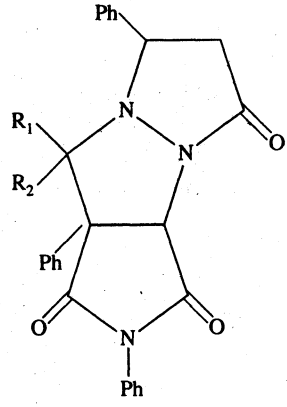
A mixture of 1,3-dipole (**4a**) and N-phenylmaleimide in benzene was heated overnight. After separation of the yellow oil, two stereoisomers (ratio 6 : 7) of 7,7-dimethyl-5,10-diphenyl-2,6,10-triazatricyclo[6.3.0.$0^{2,6}$] undecane-3,9,11-trione (**10a**) (86% yield) were obtained.

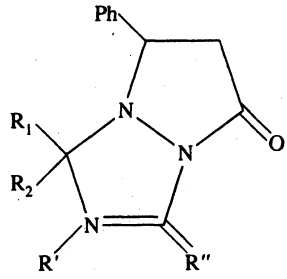
Although the constitution of each of these compounds was rigorously established from their spectral data, their relative stereochemistries could not be determined. Alkynes are found to be suitable dipolarophiles for cycloaddition reactions with 1,3-dipoles[2]. Thus, treatment of product (**4a**) with dimethyl-

acetylenedicarboxylate gave 2,2-dimethyl-3,4-di(methoxycarbonyl)-8-phenyl-1,5-diazabicyclo[3.3.0]oct-3-en-6-one **(11a)** (90% yield) as yellow crystals, m.p. 180–182°C. On the basis of a consideration of its spectral data the 1 : 1 adduct was assigned the general structure **(11a)**. In similar fashion treatment of the 1,3-dipole **(4a)** with ethyl propiolate gave 2,2-dimethyl-3-ethoxycarbonyl-8-phenyl-1,5-diazabicyclo [3,3,0] oct-3-en-6-one (97% yield) as yellow crystals, m.p. 170–172°C. The spectral data for this product **(12a)** is compatiable with it being a 1,3-dipole cycloadduct. The ^{1}H NMR spectrum of the crude product from this reaction is related to the presence of only regioisomer **(12a)**.

In view of the results obtained from the reaction of 1,3-dipole **(4a),** it was







9(a) $R_1 = R_2 = Me$
9(b) $R_1 = R_2 = Ph$
9(c) $R_1 = H, R_2 = Ph$

10(a) $R_1 = R_2 = Me$
10(b) $R_1 = R_2 = Ph$

11(a) $R_1 = R_2 = Me$
11(b) $R_1 = R_2 = Ph$
$R' = R'' = CO_2Me$

12(a) $R_1 = R_2 = Me$
12(b) $R_1 = R_2 = Ph$
12(c) $R_1 = H, R_2 = Ph$
$R' = R'' = CO_2Et$

decided to investigate the effect of a variation of substituens on the azomethine imine 1,3-dipole. Thus, the analogous diphenyl-substituted azomethine imine **(4b)** was prepared with the reaction of the known thiobenzophenone[8] and 5-phenylpyrazolidine-3-one **(3)**. The desired azomethine imine **(4c)** was also prepared according to the literature[3,9]. It is interesting to note that the reactions of both 1,3-dipoles (**4b** and **4c**) were almost compatible with the products obtained from the reaction of 1,3-dipolar **(4a)** according to their spectroscopic data.

EXPERIMENTAL

Melting points were determined with a Kofler hot-state apparatus. IR spectra were recorded on a Perkin-Elmer 157G grating-infrared spectrophotometer in the chloroform unless otherwise stated. Mass spectra were recorded with an A.E.I. MS-12 or a Kratos MS-25 low-resolution spectrometer. High-resolution mass

spectra were detemined with a Kratos M-80 spectrometer. ^1H NMR spectra were recorded with either Perkin-Elmer R34 (220 MHz) or with a Bruker WH-400 (400 MHz) spectrometer in $CDCl_3$ unless otherwise stated with tetramethylsilane as internal standard. High-pressure liquid chromatography (HPLC) was performed on a 25 cm spherisorb (5 μ) column using a water chromatography pump, model M6000, coupled *via* a U6K injector to a Cecil CE212 UV monitor and Waters Differential Refractometer R401. Medium Pressure Liquid Chromatography (MPLC) was accomplished on Jobling columns with a (2.5 × 25 cm) per column and a (2.5 × 100 cm) main column packed with 60 μ silicagel (type 60) with a Metering Pumps Limited pump, a Cecil 202 UV spectrometer and a Chemlab 270 fraction collector.

Preparation

Anhydro(I-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) (4a)

A mixture of 5-phenylpyrazolidin-3-one **(3)** (14 g, 86 mmol) and acetone (100 g, 1.7 mol) in ethanol (200 mL) was heated gently on a steam bath overnight, allowed to cool to room temperature and concentrated. The resulting yellow solid was recrystallised from ethyl acetate giving anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4a)** (12.6 g, 72%) as colourless crystals, m.p. 175–177°C. (Found: C, 71.1; H, 7.1; N, 13.7; $M^{\ddagger}$, 202. $C_{12}H_{14}N_2O$ requires: C, 71.3; H, 7.0; N, 13.85; M, 202). ν_{max} 3000, 1665, 1600, 1295, 1215 and 925 cm^{-1}; δ_H 7.15–7.45 (5H, m, 5 × ArH), 5.56 (1H, dd, J9 and 3Hz, H-5), 3.37 (1H, dd, J 17 and 9 Hz, H-4), 2.58 (1H, dd, J 17 and 3 Hz, H-4, 2.37 (3H, s, —CH_3), and 2.00 (3H, s, —CH_3).

Anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) (4b)

A mixture of thiobenzophenone (1.6 g, 8 mmol) and 5-phenylpyrazolidin-3-one **(3)** (1.0 g, 6 mmol) in chloroform (40 mL) was heated under reflux and nitrogen for 24 h, allowed to cool to room temperature and concentrated. The residual blue solid was recrystallised from ethylmethyl ketone giving anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4b)** (1.85 g, 92%) as yellow crystals, mp. 230–232°C. (Found: C, 81.0; H, 5.6; N, 8.8%; $M^{\ddagger}$, 326; $C_{22}H_{18}N_2O$ requires: C, 80.9; H, 5.6; N, 8.7%; M, 326). ν_{max} (Nujol) 1650, 1530, 1295, 1265, 1090 and 685 cm^{-1}; δ_H 8.03 (2H, dd, J 7 and 1.5 Hz, 3 × *ortho*-ArH), 6.73–7.43 (13H, m. 13 × ArH), 5.76 (1H, dd, J 10 and 3 Hz, H-5), 3.31 (1H, dd, J 16.5 and 10 Hz, H-4), and 2.62 (1H, dd, J 16.5 and 3 Hz, H-4).

Anhydro(1-benzylidene-3-oxo-5-phenylpyrazolidinium hydroxide) (4c)

To a solution of 5-phenylpyrazolidin-3-one **(3)** (40 g, 0.24 mol) in ethanol (300 mL) and water (400 mL) was added benzaldehyde (35 g, 0.33 mol) and concentrated sulphuric acid (3 mL). The mixture was stirred at room temperature for 30 min. Then the mixture was stored at 0°C for 6 h and the resulting colourless crystalline solid collected, washed twice with water and recrystallised from

ethanol to give anhydro(1-benzylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4c)** as colourless crystals, mp. 190–193°C [lit. 200–201°C][3, 9].

2, 2-Dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]octan-6-one (5a)

A solution of anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4a)** (1.01 g, 5.0 mmol) and methylacrylate (0.43 g, 5 mmol) in dry benzene (65 mL) was heated under reflux for 36 h, allowed to cool to room temperature, and concentrated giving a colourless solid which was shown by ^{1}H NMR to consist of two products in the ratio 7 : 1. Recrystallization from ethanol gave 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]octan-6-one **(5a)** (1.33 g, 87%) as yellow crystals, m.p. 115–117°C. (Found: C, 72.2; H, 5.7; N, 8.4%; M‡, 288; $C_{16}H_{20}N_2O_3$ requires: C, 72.4; H, 5.8; N, 8.1%; M, 288)ν_{max} (KBr) 2970, 1720, 1495, 1310, 945, 775 and 710 cm^{-1}, δ_H 7.23–7.53 (5H, m, 5 × ArH), 4.40 (1H, dd, J 12 and 8Hz, H-8), 4.28 (1H, broadended d, J 11 Hz, H-4). 3.80 (3H, s, —OCH_3), 3.01 (1H, dd, J 16 and 8 Hz, H-7), 2.91 (1H, ddd, J 16, 12 and 1.5 Hz, H-7), 2.65 (1H, dd, J 13 and 11 Hz, H-3), 2.20 (1H, dd, J 13 and 2 Hz, H-3), 1.25 (3H, s, —CH_3) and 0.77 (3H, s, CH_3). Attempts to obtain the minor product from the mother liquor by recrystallization or preparative T.L.C were not successful. However, seaparation of the mother liquor by HPLC using ethyl acetate: 60 : 80 ligroin = 1 : 1 as eluant gave another isomer of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]-octan-6-one **(6a)** as a colourless solid, mp. 105–107°C. (Found: M‡, 288.1482. $C_{16}H_{20}N_2O_3$ require M, 288.1474). δ_H 7.27–7.46 (5H, m, 5 × ArH), 4.20 (1H, t, J 9.5 Hz, H-8), 4.01 (1H, dd, J 11 and 9 Hz, H–3), 3.74 (3H, s, —OCH_3), 3.55 (1H, dd, J 11 and 9 Hz, H-3), 3.32 (1H, t, J 9 Hz, H–4), 3.61 (1H, dd, J 16.5, and 9.5 Hz, H-7), 2.77 (1H, dd, J 16.5 and 9.5 Hz, H–7), 1.11 (3H, s, —CH_3), and 0.98 (3H, s, CH_3).

2, 2-Dimethyl-4-ethoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]octan-6-one (5b)

A solution of anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4a)** (1.01 g, 5.0 mmol) and ethyl acrylate (2.5 g, 25 mmol) in dry benzene (40 mL) was heated under reflux for 14 h, allowed to cool to room temperature and concentrated. The residual colourless solid was shown by ^{1}H NMR to consist of two products in the ratio 6 : 1. Recrystallization from ethanol gave 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1-5-diazocyclo[3.3.0]octan-6-one **(6b)** (1.40 g, 85%) as colourless crystals, m.p. 140–142°C. (Found: C, 67.60; H, 7.30; N, 9.50%; M‡, 302; $C_{17}H_{22}N_2O_3$ requires: C, 67.60; H, 7.30; N, 9.3%; M, 302). ν_{max} (Nujol) 1690, 1470, 1465, 1375, 1185, 1095, 764 and 705 cm^{-1}; δ_H 7.03–7.55 (5H, m, 5 × ArH), 4.41 (1H dd J 12 and 8 Hz, H-8), 4.32 (1H, dd, J 11 and 3 Hz, H-4), 4.28 (2H, q, J 8 Hz, —OCH_3), 2.98 (1H, dd, J 17 and 12 Hz, H-7), 2.91 (1H, ddd, J 17, 8 and 1.5 Hz, H-7), 2.67 (1H, dd, J 13 and 11 Hz, H-3), 2.20 (1H, dd, J 13 and 3 Hz, H-3), 1.32 (3H, t, J 8 Hz, —OCH_3), 1.16 (3H,

s, CH_3—CH_2),and 0.80 (3H, s, CH_3—C_2). Attempt to obtain the minor products from the mother liquors by recrystallisation or preparative TLC were not successful. However, separation of the mother liquors by HPLC using ethyl acetate 60 : 80 ligroin = 3 : 2 as eluant gave another isomer of 2,2-dimethyl-4-ethoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]octan-6-one **(6b)** as a colourless solid, m.p. 125–127°C. (Found: M^+, 302.1644.;$C_{17}H_{22}N_2O_3$ requires: M, 302.1631), ν_{max} (Nujol) 1725, 1680, 1465, 1375, 1195 and 695 cm^{-1}; δ_H 7.17–7.47 (5H, m, 5 × ArH), 4.21 (1H, t, J 9 Hz, H–8), 4.14–4.28 (2H, m, —OCH_2CH_3), 4.01 (1H, ddd, J 13, 9 and 1 Hz, H–3), 3.55 (1H, ddd, J 13, 9 and 1 Hz, H-3), 3.30 (1H, t, J 9 Hz, H-4), 3.03 (1H, dd, J 17 and 9 Hz, H-7), 2.8 (1H, ddd, J 17, 9 and 1 Hz, H-7), 1.28 (3H, t J, 8 Hz, —OCH_2CH_3), 1.14 (3H, s, CH_3—CH_2) and 0.99 (3H, s, CH_3—C_2).

4-Methoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]octan-2-one (5c)

A mixture of anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4b)** (0.163 g, 0.5 mol) and methyl acrylate (0.860 g, 1 mmol) in dry benzene (20 mL) was heated under reflux and nitrogen for overnight, allowed to cool to room temperature, and concentrated. The residue which was shown by ^1H NMR to consist of a single compound was recrystallised from ethanol giving 4-methoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]octan-2-one **(5c)** (0.190 g, 95%) as colourless crystals, m.p. 233–235°C. (Found: M^+, 412.1774; calculated for $C_{26}H_{24}N_2O_3$: M, 412.1787). ν_{max} (Nujol) 1735, 1690, 1340, 1235, 1195, 1055 and 695 cm^{-1}; and δ_H 7.05–7.75 (15H, m, 15 × ArH), 4.68 (1H, dd, J 8 and 3 Hz, H-4), 4.15 (1H, d, J 10 Hz, H-8), 3.65–3.98 (2H, m, 2 × H-3), 3.6 (3H, s, —OCH_3), 1.91 (1H, d, J 17 Hz, H-7) and 1.18 (1H, dd, J 17 and 10 Hz, H-7).

Reaction of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo-[3.3.0]octan-6-one (5a) with Diazabicyclo [4.3.0]non-5-ene (DBN)

A solution of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo-[3.3.0]octan-6-one **(5a)** (0.100 g, 0.35 mmol) and DBN (0.200 g, 1.6 mmol) in dry benzene (20 mL) was stirred under nitrogen at room temperature for 24 h and then concentrated. The residual yellow oil product was identified as the starting material by HPLC comparison with authentic sample. Separation of the crude mixture after removal of most of the excess DBN by distillation (kugelrohr, 80–100°C/8 torr), by HPLC using ethyl acetate; 60 : 80 ligroin = 7 : 3 as eluant afforded 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo[3.3.0]octan-6-one **(5a)** as a colourless solid which was identified by comparison with an authentic sample.

Reaction of 4-methoxycarbonyl-2,2,8-triphenyl-1.5-diazabicyclo[3.3.0] octan-2-one (5c) with Diazabicyclo[4.3.0]non-5-ene (DBN)

A solution of 4-methoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]-

octan-2-one **(5c)** (0.080 g, 0.19 mmol) and DBN (0.124 g, 1 mmol) in dry benzene (20 mL) was stirred under nitrogen at room temperature for 48 h and then concentrated. The residual yellow oil, which consisted of two isomers in approximate ratio 2 : 3 separated by preparative T.L.C. using ethyl acetate: 60 : 80 ligroin = 1 : 2 as eluant in two fractions. Fraction 1 ($R_f = 0.6$) gave 4-methoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]octan-2-one **(5c)** (0.350 g, 44%) as colourless crystals which were identical with an authentic sample. Fraction 2 ($R_f = 0.5$) gave 4-methoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo-[3.3.0]octan-2-one **(6c)** (0.04 g) as a yellow oil. (Found: $M^{\ddagger}$, 412.1787; $C_{26}H_{24}N_2O_3$ require: M, 412.1787). ν_{max} (Nujol) 2920, 1730, 1685, 1600, 1490, 1230 and 945 cm^{-1}, δ_H 7.04–7.72 (15H, m, 15 × ArH), 4.45 (1H, dd, J 12.5 and 9.5 Hz, H-3), 4.26 (1H, t, J 9.5 Hz, H-8), 4.12 (1H, dd, J 9.5 and 2 Hz, H-4), 3.99 (1H, dd, J 12.5 and 2 Hz, H-3), 3.01 (3H, s, —OCH_3), 1.93 (1H, d; J 18 Hz, H-7) and 1.25 (1H, dd, J 18 and 9.5 Hz, H-7).

Reduction of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo [3.3.0]octan-6-one (5a)

A mixture of 2,2-dimethyl-4-methoxycarbonyl-8-phenyl-1,5-diazocyclo-[3.3.0]octan-6-one **(5a)** (0.15 g, 0.52 mmol) and 10% palladium on charcoal (0.40 g) in ethyl acetate (35 mL) was stirred under an atmosphere of hydrogen at room temperature. After uptake of one molar equivalent of hydrogen, the reaction mixture was filtered and concentrated giving 4-methyl-4-(5′-phenylpyrazolidin-3′-on-1′-yl)pentanoate **(7a)** (0.12 g, 80%) as a colourless oil. (Found: $M^{\ddagger}$, 290.1635; $C_{16}H_{22}N_2O_3$ require: M, 290.1631). ν_{max} (neat) 3225, 2965, 1750, 1650, 1455, 1195 and 700 cm^{-1}, δ_H 7.05–7.32 (5H, m × ArH), 4.70 (1H, t, J 8 Hz, H-5′), 4.15 (1H, bs, —NH), 3.67 (3H, s, —OCH_3), 2.7–3.2 (4H, m, 2 × —CH_2—), 2.25 (1H, dd, J 12 and 8 Hz, H-4′), 1.72 (1H, dd, J 12 and 8 Hz, H-4′), 1.20 (3H, s, —CH_3) and 0.90 (3H, s, —CH_3).

Reduction of 2,2,-dimethyl-4-ethoxycarbonyl-8-phenyl-1,5-diazocyclo-[3.3.0]octan-6-one (5b)

A mixture of 2,2-dimethyl-4-ethoxycarbonyl-8-phenyl-1,5-diazocyclo [3.3.0]-octan-6-one **(5b)** (0.202 g, 0.67 mmol) and 10% palladium on charcoal (0.50 g) in ethyl acetate (35 mL) was stirred under an atmosphere of hydrogen at room temperature. After the uptake of one molar equivalent of hydrogen, the reaction mixture was filtered and concentrated giving ethyl 4-methyl-4(5′-phenylpyrazolidin-3′-on-1′-yl)pentanoate **(7b)** (0.170 g, 48%) as a yellow oil. (Found: $M^{\ddagger}$, 304.1783; $C_{17}H_{24}N_2O_3$ requires: M, 304.1787). ν_{max}(neat) 3225, 2970, 1745, 1650, 1455, 1185 and 700 cm^{-1}, δ_H 7.10–7.40 (5H, m, 5 × ArH), 4.73 (1H, t, J 9 Hz, H-5′), 4.21 (2H, q, J 7 Hz, —OCH_2CH_3), 4.02–4.14 (1H, bs, —NH), 2.78–3.03 (4H, m, 2 × —CH_2), 2.33 (1H, dd J 12 and 9 Hz, H-4′). 1.75 (1H, dd, J 12 and 9 Hz, H-4′), 1.28 (3H, t, J 7 Hz, —OCH_2CH_3), 1.27 (3H, s, —CH_3) and 0.98 (3H, s, CH_3).

2,2-Dimethyl-3,8-diphenyl- 1,3,5-triazabicyclo[3.3.0]octane-4,6-dione (9a)

A solution of anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4a)** (0.202 g, 1 mmol) and phenyl isocyanate (0.140 g, 1.1 mmol) in dry benzene (15 mL) was heated under reflux for 5 h. The reaction mixture was cooled to room temperature and concentrated. Crystallization of the residue from ethanol gave 2,2-dimethyl-3,8-diphenyl-1,3,5-triazabicyclo[3.3.0]octane-4, 6-dione **(9a)** (0.245 g, 76%) as colourless crystals, m.p. 175–177°C. (Found: C, 70.70; H, 5.70; N, 12.85; $M^{\ddagger}$, 321., $C_{19}H_{19}N_3O_2$ requires and C, 71.00; H, 6.00; N, 13.10; M, 321). ν_{max} (Nujol) 2930, 1795, 1700, 1465, 1380 and 725 cm^{-1}, δ_H (D_5-pyridine) 7.27–7.67 (10H, m, 10 × ArH), 4.73 (1H, t, J 9Hz, H-8) and 3.02 (2H, d, J 9 Hz, 2 × –7).

2,2,3,8-Tetraphenyl-1,3,5-triazabicyclo[3.3.0]octane-4,6-dione (9b)

A solution of anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4b)** (0.163 g, 0.5 mmol) and phenyl isocyanate (0.119 g, 1 mmol) in dry benzene (25 mL) was heated under reflux and nitrogen for overnight, allowed to cool to room temperature, and concentrated. The residual yellow oil giving 2, 2,3,8-tetraphenyl-1,3,5-triazabicyclo[3.3.0]octane-4,6-dione **(9b)** as yellow oil; δ_H 6.75–7.62 (20 H, m, 20 × ArH), 3.77 (1H, dd, J 11 and 8.5 Hz, H-8), 2.75 (1H, dd, J 17 and 11 Hz, H-7), and 2.5 (1H, dd, J 17 and 8.5 Hz, H-7).

2,3,8-Triphenyl-1,3,5-triazabicyclo[3.3.0]octane-4,6-dione (9c)

A solution of anhydro(1-benzilidene-3-oxo-5-phenylpyrazolidinium hydroxide **(4c)** (0.25 g, 1 mmol) and phenyl isocyanate (0.18 g) in xylene (20 mL) was heated under reflux for 20 h, allowed to cool to room temperature and concentrated. The residual solid was recrystallised from chloroform giving 2,3, 8-triphenyl-1,3,5-triazabicyclo[3.3.0]octane-4,6-dione **(9c)** (0.23 g, 62%) as colourless crystals, mp. 227–230°C [lit. 223–224°C][10].

7,7-Dimethyl-5,10-diphenyl-2,6,10-triazabicyclo[6.3.0.$0^{2,6}$]undecane-3,9,11-tri-one (10a)

A solution of anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide **(4a)** (0.303 g, 1.5 mmol) and N-phenylmaleimide (0.520 g, 3.0 mmol) in dry benzene (30 mL) was heated under reflux for overnight, allowed to cool to room temperature and concentrated. The residual yellow oil was separated by preparative T.L.C using ethyl acetate: 60/80 ligroin = 1 : 1 as eluant in two fractions:

Fraction 1 (R_f = 0.3) after crystallisation from ethanol gave the first isomer of 7,7-dimethyl-5,10-diphenyl-2,6,10-triazabicyclo [6.3.0.$0^{2,6}$] undecane-3,9,11-trione **(10a),** m.p. 223–225°C. (Found: C, 70.6; H, 5.4; N, 11.3%; $M^{\ddagger}$, 375; $C_{22}H_{21}N_3O_3$ require: C, 70.40; H, 5.46; N, 11.20%; M, 375). ν_{max} (Nujol) 1740, 1725, 1705, 1380, 1195, 740 and 705 cm^{-1}; δ_H 7.15–7.55 (10H, m, 10 × ArH), 4.96 (1H, d, J 9 Gz, H-1), 4.42 (1H, t, J 8 Hz, H-5), 3.66 (1H, d, J 9 Hz, H-8), 2.83–3.04 (2H, m, 2 × H-4), 1.20 (3H, s, —CH3) and 0.98 (3H, s, —CH_3).

Fraction 2 ($R_f = 0.2$) after crystallisation from ethanol gave the second isomer of 7,7-dimethyl-5,10-diphenyl-2,6,10-triazabicyclo[6.3.0.$0^{2,6}$]undecane-3,9,11-tri-one **(10a)** (0.250 g, 52%) as yellow crystals, m.p. 110–112°C. (Found: C, 69.70; H, 5.60; N, 10.60%; $M^{\ddagger}$, $C_{22}H_{21}N_3O_3$ require: C, 70.40; H, 5.46; N, 11.20% M, 375) ν_{max} (Nujol) 1730, 1500, 1470, 1380, 1200, 745 and 705 cm^{-1}; δ_H 7.10 (10H, m, 10 × ArH), 5.12 (1H, d J 7 Hz, H-1), 4.3 (1H, dd, J 10 and 4.5 Hz, H-5), 3.21 (1H, d, J 7 Hz, H-8), 3.12 (1H, dd, J 17 and 10 Hz, H-4), 2.14 (1H, dd, J 17 and 4.5 Hz, H-4), 1.20 (3H, s, —CH_3), and 1.12 (3H, s, —CH_3).

5,7,7,10-Tetraphenyl-2,6,10-triazabicyclo[6.3.0.$0^{2,6}$]undecane-3,9,11-tri-one (10b)

A mixture of anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide **(4b)** (0.163 g, 0.5 mol) and N-phenylmaleimide (0.173 g, 1 mmol) in dry benzene (20 mL) was heated under reflux and nitrogen for 24 h. It was allowed to cool to room temperature and concentrated. The residual yellow oil was separated by preparative TLC using ethyl acetate: 60/80 ligroin = 1 : 2 as eluant in two fractions:

Fraction 1 ($R_f = 0.3$) after crystallization from ethanol gave the first isomer of 5,7,7,10-tetraphenyl-2,6,10-triazabicyclo[6.3.0.$0^{2,6}$]undecane-3,9,11-tri-one **(10b)** (0.150 g, 61%) as colourless crystals, mp. 155–157°C. (Found: $M^{\ddagger}$, 499.1893; Calculated for $C_{32}H_{25}N_3O_3$: M, 499.1895). ν_{max} (Nujol) 1720, 1490, 1210, 750 and 695 cm^{-1}; δ_H ($CDCl_3/C_6D_6$) 6.72–7.55 (20 H, m, 20 × ArH), 5.36 (1H, d, J 7 Hz, H-1), 4.14 (1H, d, J 9.5 Hz, H-5), 3.88 (1H, d, J 7 Hz, H-8), 1.75 (1H, d, J 17 Hz, H-4) and 1.17 (1H, dd, J 17 and 9.5 Hz, H-4).

Fraction 2 ($R_f = 0.2$) after crystallization from ethanol gave the second isomer of 5,7,7,10-tetraphenyl-2,6,10-triazabicyclo[6.3.0.$0^{2,6}$]undecane-3,9,11-tri-one **(10b)** (0.90 g, 36%) as colourless crystals, m.p. 223–225°C. (Found: $M^{\ddagger}$, 499.1927; calculated for $C_{32}H_{25}N_3O_3$: M, 499, 1896), ν_{max} 2990, 1740, 1680, 1600, 1495, 1445, 1360, 1170, 1060 and 960 cm^{-1}; δ_H 6.60–7.25 (20 H, m, 20 × ArH), 5.27 (1H, d, J 8 Hz, H-1), 4.75 (1H, dd, J 9 and 4 Hz, H-5), 4.02 (1H, d, J 8 Hz, H-8), 3.26 (1H dd, J 17 and 9 Hz, H-4) and 2.52 (1H, dd, J 17 and 4 Hz, H-4).

2,2-Dimethyl-3-4-di(methoxycarbonyl)-8-phenyl-1,5-diazabicyclo[3.3.0]-oct-3-en-6-one (11a)

A solution of anhydro(1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide **(4a)** (0.202 g, 1 mmol) and dimethyl acetylenedicarboxylate (0.248 g, 2 mmol) in dry benzene (20 mL) was heated under reflux for overnight, allowd to cool to room temperature and concentrated. The oily yellow residue was crystallized from ethanol giving 2,2-dimethyl-3-4-di(methoxycarbonyl)-8-phenyl-1,5-diazabicyclo[3.3.0]oct-3-en-6-one **(11a)** (0.308 g, 90%). m.p. 180–182°C. (Found: C, 62.90; H, 5.70; N, 8.20; $M^{\ddagger}$, 344; $C_{18}H_{20}N_2O_5$ require: C, 62.80; H, 5.90; N, 8.10; M, 344). ν_{max} (Nujol) 2900, 1755, 1615, 1465, 1380 and 1075 cm^{-1}; δ_H 7.26–7.55 (5H, m, 5 × ArH), 4.62 (1H, t, J 10 Hz, H-8), 3.95 (3H, s, —CO_2Me), 3.70 (3H, s, —CO_2Me), 2.94 (2H, d, J 10 Hz, 2 × H-7), 1.40 (3H, s, CH_3—CH_2) and 1.21 (3H, s, CH_3—C_2).

3,4-Di(methoxycarbonyl)-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]oct-3-en-6-one (11b)

A mixture of anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4b)** (0.163 g, 0.5 mol) and acetylenedicarboxylate (0.14 g, 1 mmol) in dry benzene (20 mL) was heated under reflux and nitrogen for overnight, allowed to cool to room temperature and concentrated. The residual mass was crystallized from ethanol giving 3,4-di(methoxycarbonyl)-2,2,8-triphenyl-1,5-diazabicyclo [3.3.0]oct-3-en-6-one **(11b)** (0.220 g, 94%) as yellow crystals, m.p. 229–231°C. (Found: $M^{\ddagger}$, 468.1665; calculated for $C_{28}H_{24}N_2O_5$: M, 468.1685). ν_{max} (Nujol) 1760, 1705, 1410, 1235, 755 and 685 cm^{-1}; δ_H 7.81 (2H, d—J 7, Hz, 2 × *ortho*-ArH), 6.93–7.42 (13 H, m, 13 × ArH) , 3.98 (3H, s, —OCH_3), (1H, dd, J 12 and 7.5 Hz, H-8), 3.47 (3H, s, —OCH_3), 2.92 (1H, dd, J 17 and 12 Hz, H-7) and 2.72 (1H, dd, J 17 and 7.5 Hz, H-7).

2,2-Dimethyl-3-ethoxycarbonyl-8-phenyl-1,5-diazabicyclo[3.3.0]oct-3-ene-6-one (12a)

A solution of anhydro (1-isopropylidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4a)** (0.101 g, 0.5 mmol) and ethyl propiolate (0.980 g, 1 mmol) in dry benzene (15 mL) was heated under reflux for 18 h, allowed to cool to room temperature and concentrated. The residual yellow oil was recrystallised from ethanol giving 2,2-dimethyl-3-ethoxycarbonyl-8-phenyl-1-5-diazabicyclo[3.3.0]-oct-3-ene-6-one **(12a)**. (0.155 g, 97%). m.p. 170–172°C. Found: C, 67.90; H, 6.56; N, 9.20; $M^{\ddagger}$, 300; $C_{17}H_{20}N_2O_3$ requires C, 68.00, H, 6.70; N, 9.30; M, 300); ν_{max} (Nujol) 2900, 1720, 1690, 1580, 1470, 1375, 1315 and 760 cm^{-1}; δ_H 7.32–7.65 (6H, m, 5 × ArH, H-4), 4.58 (1H, t, J 9 Hz, H-8), 4.17 (2H, q, J 7 Hz,OCH_2CH_3), 2.95 (2H, d, J 9 Hz, 2 × H-7), 1.33 (3H, s, CH_3—C_2), 1.26 (3H, t, J 7 Hz, —OCH_2CH_3) and 1.24 (3H, s, CH_3—C_2).

3-Ethoxycarbonyl-2,2,8-triphenyl-1,5-diazabicyclo[3.3.0]oct-3-ene-6-one(12b)

A mixture of anhydro(1-diphenylmethylene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4b)** (0.163 g, 0.5 mol) and ethyl propiolate (0.980 g, 1 mmol) in dry benzene (20 mL) was heated under reflux and nitrogen for 24 h. It was recrystallised from ethanol and gave the 3-ethoxycarbonyl-2,2,8-triphenyl-1, 5-diazabicyclo[3.3.0]oct-3-ene-6-one **(12b)** (0.205 g, 97%) as yellow crystals, m.p. 145–147°C. (Found: C, 76.5; H, 5.58; N, 6.3%; $M^{\ddagger}$, 424; $C_{27}H_{24}N_2O_3$ requires: C, 76.40; H, 5.79; N, 6.30%; M, 424). ν_{max} (Nujol) 1695, 1590, 1410, 1315, 1200, 1065, 755, 705 and 690 cm^{-1}; δ_H 7.85 (2H, d, J 7 Hz, 2 × *ortho*-ArH), 3.48–4.12 (2H, m, —OCH_2CH_3), 3.65 (1H, dd, J 12.5 and 7.5 Hz, H-8), 2.91 (1H, dd, J 17.5 and 12.5 Hz, H-7), 2.71 (1H, dd, J 17.5 and 7.5 Hz, H-7), and 1.08 (3H, t, J 7 Hz, —OCH_2CH_3).

2,8-Diphenyl-3-ethoxycarbonyl-1,5-diazabicyclo[3.3.0]oct-3-ene-6-one (12c)

A mixture of anhydro (1-benzilidene-3-oxo-5-phenylpyrazolidinium hydroxide) **(4c)** (1.5 g, 6 mmol) and ethyl acetate (1.0 g, 10 mmol) in dry benzene (6.0 mL) was heated under reflux overnight, allowed to cool to room temperature and

concentrated. The residual oil was recrystallised from ethanol giving 2,8-diphenyl-3-ethoxycarbonyl-1,5-diazabicyclo[3.3.0]oct-3-ene-6-one **(12c)** (1.7 g, 81%) as colourless crystals, mp. 195–197°C. (Found: C, 66.3; H, 7.10; N, 9.70%; $M^{\ddagger}$, 348; $C_{21}H_{20}N_2O_3$ requires: C, 66.30; H, 7.00; N, 9.70%; M, 348). ν_{max} (Nujol) 1725, 1695, 1605, 1255 and 1165 cm^{-1}; δ_H 7.63 (1H, s, H-4), 7.02-7.35 (10H, m, 10 × ArH), 5.23 (1H, s, H-2), 4.42 (1H, dd, J 12 and 8 Hz, H-8), 3.95–4.15 (2H, m, —O—CH_2), 2.84–3.06 (2H, m, 2 × H-7) and 1.12 (3H, t, J 8 Hz, —CH_3).

REFERENCES

1. Huisgen, *Angew. Chem. Int. Ed. Engl.*, **2**, 565 (1963).
2. H. Dom and A. Otto, *Ber.*, **101**, 3387 (1968).
3. E. Muckemann; *Ber.* **42**, 3449 (1909); *J. Prakt. Chem.*, 83 (1911).
4. D.S. Kemp, M.D. Sidell and T.J. Shortridge, *J. Org. Chem.*, **44**, 4473 (1979).
5. F.D. Greene, M.A. Berwich and J.C. Stowell, *J. Am. Chem. Soc.*,**92**, 867 (1970).
6. H.H. Wasserman and H. Matsuyama, *J. Am. Chem. Soc.*, **103**, 461 (1981).
7. H.A. Szymanski and N.L. Alpert, Theory and Practice of Infrared Spectroscopy, New York, Ch. 5, pp. 288–294 (1964).
8. A. Schonberg, O. Schutz and S. Nickel, *Ber.*, **61**, 1375 (1928).
9. W.O. Godtfredsen and S. Vangedal, *Acta Chem. Scand.*, **9**, 1498 (1995).
10. D. Alker; Sheffield University (unpublished result).

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