Novel cycloadducts from the 1,3-dipolar cycloaddition reactions of triazolium-1-imide 1,3-dipoles

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Dedicated to Tony McKervey on the occasion of his 65th birthday

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Abstract

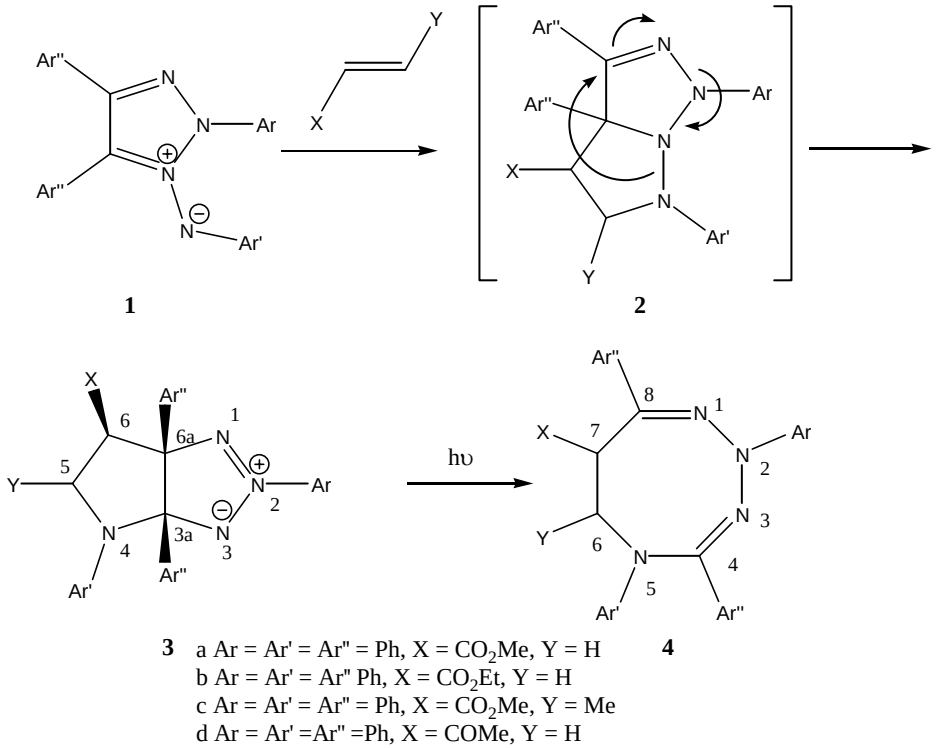
A range of imidazo-1,2,3-triazoles were synthesised by the 1,3-dipolar cycloaddition of triazolium-1-imides with N-sulfonyl imines. Oxazolo-1,2,3-triazoles were identified as side products of this reaction. Benzyne was also used as a 1,3-dipolarophile in the cycloaddition reaction, resulting in a range of tricyclic triazoloindoles.

Keywords: 1,3-Dipolar cycloaddition, N-sulfonyl imines, benzyne

Introduction

In work previously carried out by our group 3a,6a-diaryl hexahydropyrrolotriazoles **3** underwent photoinduced disrotatory ring expansion to the new 2,5,6,7-tetrahydro-1,2,3,5 tetrazocines **4**[1] (Scheme 1). Of key importance in the stability of these tetrazocines was the saturation of the C-6 position, and the nature of the group attached to C-6. Both saturation and electron withdrawing groups were found to initiate rearrangement of the initially formed tetrazocine, by the attack of N-2 on C-6. In searching for new ring systems of this type, and in particular those with a fifth nitrogen in the system, the cycloadditions of triazolium-1-imides **1** with various dipolarophiles were investigated.

The cycloadditions of triazolium-1-imides with various alkene and alkyne dipolarophiles have been extensively studied.[2] On addition, the initial bicyclic adducts **2** subsequently undergo a 1,4-sigmatropic rearrangement to give the bicyclic 1,2,3-triazoles **3**.



3 a Ar = Ar' = Ar'' = Ph, X = CO_2Me, Y = H
b Ar = Ar' = Ar'' Ph, X = CO_2Et, Y = H
c Ar = Ar' = Ar'' = Ph, X = CO_2Me, Y = Me
d Ar = Ar' =Ar'' =Ph, X = COMe, Y = H

Scheme 1. 1,3-Dipolar cycloaddition of trizolium-1-imides, followed by 1,4-sigmatropic rearrangement. The resulting bicyclic compounds undergo photo-induced ring expansion to give the novel 1,2,3,5-tetrazocines.

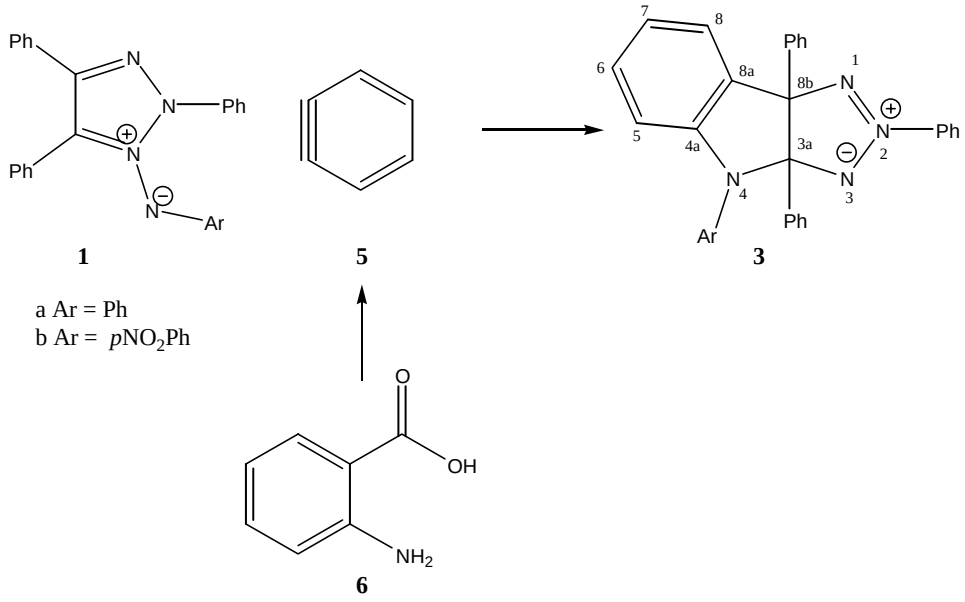
Results and Discussion

Benzyne as a Dipolarophile.

The use of benzyne **5** as a dipolarophile in the cycloaddition with triazolium-1-imide **1** would provide a degree of unsaturation between C-4a and C-8a in the cycloadduct **3** (Scheme 2). Subsequent photochemical induced ring opening would produce a 1,2,3,5-tetrazocine **4** with a C-5a-C-9a double bond, but attack by N-2 on a closed aromatic sextet of electrons would be a highly unfavourable process.

In situ formation of benzyne through diazotisation of anthranilic acid **6** and isoamylnitrite in 1,2-dimethoxyethane with the 1,3-dipole **1a,b** yielded the cycloadducts **3a,b**. Reaction conditions were optimised by heating a stirred solution of the 1,3-dipole at the reflux temperature of the solvent, thereby increasing the reactivity of the dipole within the short transitory lifetime of benzyne. Similarly, it was observed that yields were maximised by simultaneous addition of solvent solutions of anthranilic acid and isoamylnitrite every five minutes in $2cm^3$ aliquots.

Yields of the cycloadduct were increased by introducing a *para* nitro-group on the phenyl ring of the nitrogen terminus of the 1,3-dipole.



Scheme 2. 1,3-Dipolar cycloaddition of benzyne to triazolium-1-imides.

N-Sulfonyl imines as dipolarophiles.

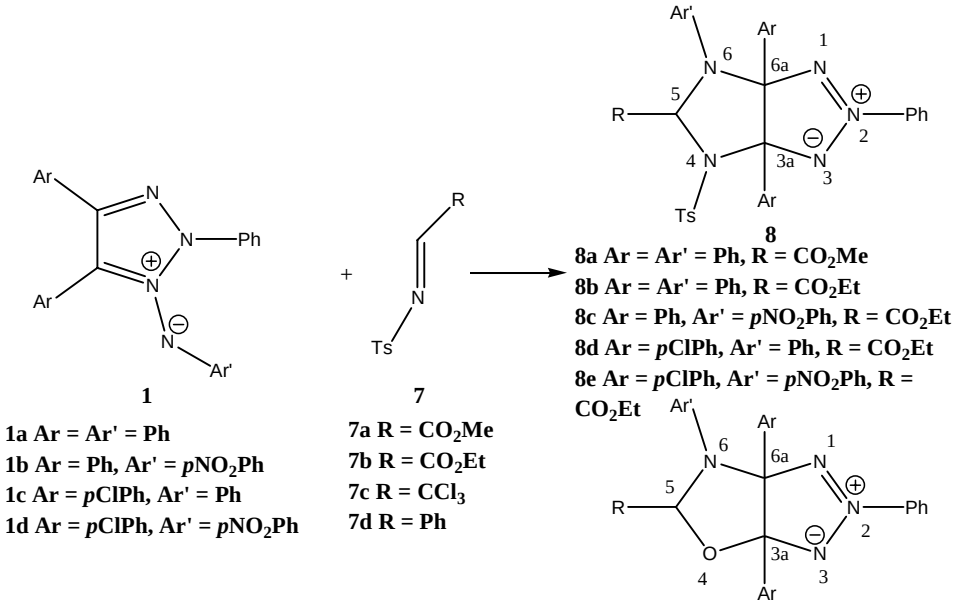
Previously the only carbon and nitrogen-containing dipolarophiles that had been successfully used in the cycloaddition to triazolium-1-imides were isocyanates and isothiocyanates.[2,3] However the use of these dipolarophiles limit the substituent at C-5 to carbonyl and thiocarbonyl groups. In order to enable variation of the substituent at C-5 a different nitrogen-containing dipolarophile was required.

N-sulfonyl imines have been increasing in importance because they are one of the few types of electron-deficient imines that are stable enough to be isolated but reactive enough to undergo addition reactions. They have been used as electron-deficient 1,3-azabutadiene equivalents in inverse electron demand Diels-Alder chemistry,[4] as electrophilic aza-aldehyde equivalents in addition reactions,[5] as reactive olefin equivalents in ene reactions,[6] and as precursors to N-sulfonyloxaziridines which have utility as chiral oxidants.[7] It was decided to investigate if N-sulfonyl imines could be used in the 1,3-dipolar cycloaddition with triazolium-1-imides.

Conjugation with electron-withdrawing or electron-releasing substituents increases the dipolarophilic activity of a multiple bond. Sulfonyl imines containing an aromatic group do not form adducts when heated in benzene with dienes, despite the electron-withdrawing effect of the sulfonyl group. However, if the carbon atom of the C=N bond also carries an electron-withdrawing group as in CO_2R, CF_3 or CCl_3, adducts are formed under the above conditions.[8]
Four imines **7a-d** were chosen to use as dipolarophiles in the cycloaddition reaction. Of these, three had an electron-withdrawing group **7a-c** attached to the carbon, i.e. CO_2CH_3, $CO_2C_2H_5$, CCl_3, and the fourth **7d** had a phenyl group attached to the carbon atom. As expected the N-sulfonyl benzaldimine failed to give the required imidazo-1,2,3-triazole. The N-sulfonyl

trichloroimine **7c** also failed to give the required adduct. However both of the N-sulfonyl imino acetic acid esters **7a,b** successfully added to the triazolium-1-imide **1a-d** to give the novel imidazo-1,2,3-triazoles **8a-e** with a saturated C-5 position (Scheme 3). The success of the addition of the imino acetic acid esters is thought to be due to favourable secondary orbital interactions in the transition state, due to the conjugation of the π-system.

In all cases, oxazolo-1,2,3-triazoles **9a-g** were isolated from the reaction mixtures. These were obtained by the hydrolysis of the N-sulfonyl imines and subsequent cycloaddition of the resulting aldehydes to the triazolium-1-imides. The use of dry solvents in inert atmosphere reduced the yield of the oxazolo-1,2,3-triazoles, but did not improve the yields of the imidazo-1,2,3-triazoles. Cycloadducts of this type were previously synthesised by the cycloaddition of aldehydes with triazolium-1-imides.[9] Compounds **9a-e**, and **9g** are new derivatives of this ring system.



1

1a Ar = Ar' = Ph
1b Ar = Ph, Ar' = *p*NO_2Ph
1c Ar = *p*ClPh, Ar' = Ph
1d Ar = *p*ClPh, Ar' = *p*NO_2Ph

7

7a R = CO_2Me
7b R = CO_2Et
7c R = CCl_3
7d R = Ph

8

8a Ar = Ar' = Ph, R = CO_2Me
8b Ar = Ar' = Ph, R = CO_2Et
8c Ar = Ph, Ar' = *p*NO_2Ph, R = CO_2Et
8d Ar = *p*ClPh, Ar' = Ph, R = CO_2Et
8e Ar = *p*ClPh, Ar' = *p*NO_2Ph, R = CO_2Et

9

9a Ar = Ar' = Ph, R = CO_2Me
9b Ar = Ar' = Ph, R = CO_2Et
9c Ar = Ph, Ar' = *p*NO_2Ph, R = CO_2Et
9d Ar = *p*ClPh, Ar' = Ph, R = CO_2Et
9e Ar = *p*ClPh, Ar' = *p*NO_2Ph, R = CO_2Et
9f Ar = Ar' = R = Ph
9g Ar = Ar' = Ph, R = CCl_3

Scheme 3. 1,3-Dipolar cycladdition of triazolium-1-imides with N-sulfonyl imines, giving novel imidazo-1,2,3-triazoles. Oxazolo-1,2,3-triazoles were identified as side-products of this reaction.

Table 1. Yields and melting points of the novel imidazo-1,2,3-triazoles and oxazolo-1,2,3-triazoles

	Ar	Ar'	R	Yield	M.P. ^{o}C
8a	Ph	Ph	CO_2Me	15%	197-198
8b	Ph	Ph	CO_2Et	26%	206-208
8c	Ph	*p*NO_2Ph	CO_2Et	18%	243-244
8d	*p*ClPh	Ph	CO_2Et	10%	228-230
8e	*p*ClPh	*p*NO_2Ph	CO_2Et	20%	168-170
9a	Ph	Ph	CO_2Me	22%	220
9b	Ph	Ph	CO_2Et	25%	154-156
9c	Ph	*p*NO_2Ph	CO_2Et	30%	179-180
9d	*p*ClPh	Ph	CO_2Et	21%	181-182
9e	*p*ClPh	*p*NO_2Ph	CO_2Et	26%	178-180
9f	Ph	Ph	Ph	50%	171-173
9g	Ph	Ph	CCl_3	46%	163-164

Experimental Section

General Procedures. Infrared spectra were measured on a Perkin-Elmer System 2000 FT-IR. NMR spectra were recorded on a Bruker 400MHz spectrometer. Melting points were recorded on a Griffin apparatus and are uncorrected. Microanalytical data was provided by the Chemistry Department in University College, Dublin. The synthesis of all dipoles[2,10] and dipolarophiles[11] was carried out as described previously.

The following is a typical procedure for the 1,3-dipolar cycloaddition using benzyne as the dipolarophile:

2,3a,4,8b-Tetraphenyl-3,3a,4,6a-tetrahydro-[1,2,3]-triazolo[4,5-b]indole (3a)

1g of the dipole was added to 30cm^3 of dimethoxyethane and the solution heated to reflux temperature. 5cm^3 of isoamylnitrite was added to a conical flask containing 15cm^3 of dimethoxyethane. Similarly a 20cm^3 solution of 3.5g of anthranilic acid in dimethoxyethane was made up. 2cm^3 of each solution was added simultaneously to the reaction through the condenser every 5 minutes. When this was complete the reaction was further heated under vigorous stirring for 25 minutes. Excess solvent and isoamylnitrite were removed under reduced pressure and the remaining oil adsorbed onto 10g of silica. The isolation of the cycloadduct was achieved by flash chromatography. (Pet.ether (60-80) 80%:diethyl ether 20%) to give 3a in 50% yield as a yellow solid. M.p. 142 ^{o}C

IR(KBr) (cm^{-1}): 1600, 1588, 1499, 761, 774, 754.

^{1}H($CDCl_3$)(ppm): 6.81-6.93 (4H,m), 6.94-7.07 (8H,m), 7.11 (1H,d), 7.15-7.28 (4H,m), 7.44-7.59(5H,m), 8.34(2H,d).
^{13}C($CDCl_3$)(ppm): 91.40, 105.42, 108.92, 125.42, 123.31, 123.97, 124.05, 127.51, 127.58, 127.80, 127.87, 128.34, 129.94, 129.20, 129.35, 129.64, 131.01, 132.05, 137.99, 139.24, 141.12, 141.56, 150.03.
Microanalysis, found (theory): C 82.56 (82.73), H 4.98 (5.20), N 12.12 (12.05)

4-(4-Nitrophenyl),2,3a,8b-triphenyl-3,3a,4,6a-tetrahydro[1,2,3]-triazolo[4,5-b]indole (3b).

The isolation of the cycloadduct was achieved by flash chromatograpy. (Pet.ether (80:20) 80%: ether 20%) to give 3b in 70% yield as a yellow solid. M.p. 158 ^{o}C
IR(KBr) (cm^{-1}): 1585, 1480, 1468, 1324, 762, 747, .685.
^{1}H($CDCl_3$)(ppm):6.84-7.21(10H,m),7.27-7.36(2H,m),7.42-7.68(7H,m),8.08(2H,m), 8.32(2H,d)
^{13}C($CDCl_3$)(ppm): 120.71, 122.80 ,123.31, 125.25, 127.81, 127.93, 128.07, 128.25, 128.31, 128.38, 128.83, 129.62, 129.83, 132.21, 132.52, 136.94, 138.09, 140.78, 142.01, 147.20, 147.41.
Microanalysis, found (theory): C 75.61 (75.42), H 4.33 (4.54), N 13.51 (13.74)

The following is a typical procedure for the 1,3-dipolar cycloaddition using N-sulfonyl imines as the dipolarophile:

2,3a,6,6a-Tetraphenyl-4-tosyl-5-methylcarbonyl-3,3a,4,5,6,6a-hexahydroimidazo-[4,5-d]-1,2,3-triazole (8a)

1,2-bis(phenylazo)stilbene (0.5g, 0.0013mol) and N-*p*-toluenesulfonyl-2-acetic acid methyl ester (0.35g, 0.0015mol) were stirred under reflux in 25cm^3 sodium dried benzene for 24 hours. The hot solution was filtered and the filtrate evaporated to dryness. The residue was purified on a silica gel column (mobile phase, 5:1 pet. ether 40-60: ethyl acetate) yielding 123mg (0.195mmol, 15%) of a yellow solid. M.p. 197-198^{o}C
^{1}H ($CDCl_3$) (ppm): 1.49 (3H, s, CH_3), 3.47 (3H, s, OCH_3), 5.22 (1H, s, C5-H), 6.80-6.84 (5H, m), 6.96, (1H, t, J=7.2Hz), 7.04, (2H, d, J=8.4Hz), 7.12, (2H, t, J=8.4Hz), 7.23, (3H, d, J=8.0Hz), 7.55-7.59 (6H, m), 7.65, (1H, d, J=7.2Hz), 7.98, (2H, d, J=8.4Hz), 8.45, (2H, d, J=8.0Hz) (all aromatic H).
^{13}C ($CDCl_3$) (ppm): 21.60 (CH_3), 53.00 (OCH_3), 76.70 (C5), 97.87, 97.92 (C3a, C6a), 122.87, 124.24, 125.52, 127.30, 127.65, 127.78, 128.52, 129.03, 129.29, 129.69, 132.81, 136.02, 144.45 (all aromatic C), 164.37 (C=O).

2,3a,6,6a-Tetraphenyl-4-tosyl-5-ethylcarbonyl-3,3a,4,5,6,6a-hexahydroimidazo[4,5-d]-1,2,3-triazole (8b). 26% yield of a yellow solid. M.p. 206-208°C
IR (KBr) (cm^{-1}): 1745, 1597, 1505, 1449, 1306, 1263, 1168, 1090, 839, 750, 690.
^{1}H (DMSO-d_6) (ppm): 1.39 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 2.20 (3H, s, CH_3), 4.39-4.43 (2H, m, $OC\mathbf{H_2}CH_3$), 5.21 (1H, s, C5-H), 6.90 (1H, t, J=7.2Hz), 6.98-7.10 (10H, m), 7.13-7.17 (4H, m), 7.45 (2H, d, J=4.8Hz), 7.61 (2H, t, 7.6Hz), 7.3 (1H, t, J=7.6Hz), 7.79 (2H, d, J=8.0Hz), 8.01 (2H, d, J=7.6Hz) (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 14.24 (CH_3), 21.31 ($OCH_2\mathbf{C}H_3$), 62.56 ($O\mathbf{C}H_2CH_3$), 75.82 (C5), 100.35, 102.27 (C3a, C6a), 120.56, 122.64, 122.76, 127.29, 127.54, 127.79, 128.03, 128.47, 128.55, 129.14, 129.67, 129.74, 132.88, 135.77, 136.02, 138.09, 139.24, 141.13, 144.27 (all aromatic C), 171.02 (C=O).
Microanalysis, found, (theory): C 69.79 (69.03), H 5.30 (5.17), N 11.16 (10.88)
2,3a,6a-Triphenyl-6-(4-nitrophenyl)-4-tosyl-5-ethylcarbonyl-3,3a,4,5,6,6a hexahydroimidazo[4,5-d]-1,2,3-triazole (8c). 18% yield of an orange solid. M.p. 243-244°C
IR (KBr) (cm^{-1}): 1739, 1597, 1472, 1450, 1540, 1310, 1175, 859.
^{1}H (DMSO-d_6) (ppm): 1.45 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 1.99 (1H, s, CH_3), 4.48 (2H, m $OC\mathbf{H_2}CH_3$), 5.55 (1H, s, C5-H), 6.93-6.97 (3H, m), 7.03-7.07 (2H, m), 7.12 (2H, t, J=4.8Hz), 7.29 (2H, t, J=8.8Hz), 7.61 (2H, t, J=8.4Hz), 7.78 (2H, t, J=8.4Hz), 7.85-7.94 (4H, m), 8.03 (2H, t, J=8.0Hz), 8.14 (2H, d, J=9.2Hz), 8.48 (2H, d, J=8.0Hz) (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 14.44 (CH_3), 21.42 ($OCH_2\mathbf{C}H_3$), 60.12 ($O\mathbf{C}H_2CH_3$), 73.15 (C5), 96.65, 97.43 (C3a, C6a), 123.12, 124.39, 124.57, 127.40, 127.63, 127.87, 128.31, 128.41, 128.81, 129.00, 129.70, 130.23, 139.22, 144.45 (all aromatic C), 173.26 (C=O).
Microanalysis, found (theory): C 64.08, (64.51), H 4.51 (4.69), N 12.47 (12.20)
2,6-Diphenyl-3a,6a-di-(4-chlorophenyl)-4-tosyl-5-ethylcarbonyl-3,3a,4,5,6,6a-hexahydroimidazo[4,5-d]-1,2,3-triazole (8d). 10% yield of an orange solid. M.p. 228-230°C
IR (KBr) (cm^{-1}): 1749, 1598, 1492, 1469, 1168, 1092, 855, 669, 768.
^{1}H (DMSO-d_6) (ppm): 1.37 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 2.19 (3H, s, CH_3), 4.38-4.43 (2H, m, $OC\mathbf{H_2}CH_3$), 5.21 (1H, s, C5-H), 6.93 (1H, t, J=7.2Hz), 7.01 (2H, d, J=7.6Hz), 7.07 (2H, d, J=8.8Hz), 7.12-7.20 (6H, m), 7.23, (2H, d, J=8.8Hz), 7.49 (2H, d, J=6.4Hz), 7.60 (2H, t, J=7.6Hz), 7.74 (1H, t, J=7.6Hz), 7.78 (2H, d, J=8.4Hz), 8.05 (2H, d, J=7.6Hz) (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 14.21 (CH_3), 21.31 ($OCH_2\mathbf{C}H_3$), 62.77 ($O\mathbf{C}H_2CH_3$), 75.67 (C5), 99.70, 101.77 (C3a, C6a), 120.67, 122.83, 123.01, 127.58, 128.33, 128.54, 129.31, 129.48, 129.67, 129.84, 133.08, 133.44, 134.98, 135.56, 137.19, 139.08, 140.65, 144.49 (all aromatic C), 171.05 (C=O).
Microanalysis, found (theory): C 62.26 (62.36), H 4.47 (4.38), N 9.80 (9.83)
2-Phenyl-3a,6a-di-(4-chlorophenyl)-6-(4-nitrophenyl)-4-tosyl-5-ethylcarbonyl-3,3a,4,5,6,6a-hexahydroimidazo[4,5-d]-1,2,3-triazole (8e). 20% yield of an orange solid. M.p. 168-170°C
IR (KBr) (cm^{-1}): 1763, 1598, 1470, 1509, 1323, 1173, 1115, 1092, 834, 685, 749.

^{1}H (DMSO-d_6) (ppm): 1.45 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 2.28 (3H, s, CH_3), 4.48-4.51 (2H, m, $OC\mathbf{H_2}CH_3$), 5.57 (1H, s, C5-H), 6.92 (2H, d, J=9.6Hz), 7.05-7.09, (2H, m), 7.21 (3H, d, J=8.8Hz), 7.30-7.35 (5H, m), 7.61 (2H, d, J=8.0Hz), 7.72 (1H, t, J=7.2Hz), 7.91 (2H, d, J=8.4Hz), 8.02-8.06 (4H, m)(all aromatic H).
^{13}C (DMSO-d_6) (ppm): 14.23 (CH_3), 21.37 ($OCH_2\mathbf{C}H_3$), 63.44 ($O\mathbf{C}H_2CH_3$), 73.21 (C5), 100.77, 101.25 (C3a, C6a), 115.96, 123.03, 125.21, 127.64, 128.58, 129.22, 129.41, 129.55, 129.74, 129.98, 133.18, 133.29, 133.84, 134.99, 135.12, 136.87, 139.16, 139.96, 144.95, 146.13 (all aromatic C), 170.78 (C=O).

The following is a typical procedure for the 1,3-dipolar cycloaddition with aldehydes acting as the dipolarophile.

2,3a,5,6,6a-Pentaphenyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9f)
1,2-bis(phenylazo)stilbene (0.4g, 0.001mol) and N-*p*-toluenesulfonyl benzaldimine (0.26g, 0.001mol) were stirred under reflux in sodium-dried benzene for 6 hours. After 6 hours a further 0.026g (0.0001mol, 10% excess) of N-p-toluenesulfonyl benzaldimine was added and the mixture allowed to reflux for a further 12 hours. The benzene was removed under vacuum and the residue was recrystallised from ethanol, yielding 0.24g (0.0005mol, 50%) of a yellow solid. M.p. 171-173^{o}C (lit. 174-175^{o}C)[9]
IR (KBr) (cm^{-1}): 1602, 1501, 1450, 763, 691.
^{1}H (DMSO-d_6) (ppm): 6.28 (1H, s, C5-H), 6.78 (3H, t, J=4Hz), 6.99 (2H, t, J=8Hz), 7.14 (6H, t, J=8Hz), 7.21 (2H, t, J=8Hz), 7.47-7.57 (5H, m), 7.68 (2H, t, J=8Hz), 7.76 (1H, t, J=8Hz), 7.93 (2H, d, J=8Hz), 8.25 (2H, d, J=8Hz), (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 91.25 (C5), 98.45, 98.49 (C3a, C6a), 112.24, 120.53, 121.70, 122.96, 126.95, 127.56, 127.77, 128.29, 129.44, 129.28, 129.86, 129.97, 132.89, 137.19, 138.28, 138.89, 140.33, 143.33 (all aromatic C).
2,3a,6,6a-Tetraphenyl-5-methylcarbonyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9a). 22% yield of a pale yellow solid. M.p. 220^{o}C
IR (KBr) (cm^{-1}): 1753, 1598, 1505, 1449 , 752, 698.
^{1}H (DMSO-d_6) (ppm): 3.97 (3H, s, OCH_3), 5.69 (1H, s, C5-H), 6.61 (2H, d, J=8.4Hz), 6.77 (1H, t, J=7.2Hz), 7.05-7.15 (10H, m), 7.45 (2H, d, J=6.4Hz), 7.64 (2H, t, J=7.2Hz), 7.73 (1H, t, J=7.2Hz), 8.22 (2H, d, J=7.6Hz) (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 53.73 (OCH_3), 86.76 (C5), 97.08, 114.78 (C3a, C6a), 115.76, 119.94, 123.01, 126.89, 127.23, 127.85, 128.35, 128.48, 128.79, 129.07, 129.89, 133.04, 136.02, 137.26, 140.22, 141.34 (all aromatic C), 170.40 (C=O).
Microanalysis, found (theory): C 72.79 (73.09), H 5.17 (5.08), N 11.65 (11.76)

2,3a,6,6a-Tetraphenyl-5-ethylcarbonyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9b). 25% yield of a yellow solid. M.p. 154-156°C

IR (KBr) (cm^{-1}): 1754, 1600, 1505, 1449, 1232, 1203, 1180, 753, 699.

^1H (DMSO-d_6) (ppm): 1.37 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 4.41-4.46 (2H, m $OC\mathbf{H_2}CH_3$), 5.65 (1H, s, C5), 6.29 (2H, d, J=8.0Hz), 6.77 (1H, t, J=7.6Hz), 7.08-7.13 (10H, m), 7.46 (2H, d, J=5.2Hz), 7.64 (2H, t, J=8.0Hz), 7.73 (1H, d, J=7.2Hz), 8.22 (2H, d, J=7.2Hz) (all aromatic H).

^{13}C (DMSO-d_6) (ppm): 14.32 ($OCH_2\mathbf{C}H_3$), 62.65 ($O\mathbf{C}H_2CH_3$), 86.96 (C5), 97.11, 114.79 (C3a, C6a), 115.73, 119.91, 123.02, 126.91, 127.25, 127.82, 128.31, 128.47, 128.78, 129.05, 129.89, 133.02, 136.09, 137.25, 140.23, 141.33 (all aromatic C), 169.86 (C=O).

Microanalysis, found (theory): C 73.08 (73.45), H 5.69 (5.34), N 10.74 (11.42)

2,3a,6a-Triphenyl-6-(4-nitrophenyl)--5-ethylcarbonyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9c). 30% yield of a yellow solid. M.p. 179-180°C

IR (KBr) (cm^{-1}): 1754, 1597, 1449, 1505, 1385, 1314, 1211, 1160, 1134, 1114, 834, 758, 702.

^1H (DMSO-d_6) (ppm): 1.41 (3H, t, J=7.2Hz, $OCH_2C\mathbf{H_3}$), 4.48 (2H, m, $OC\mathbf{H_2}CH_3$), 5.95 (1H, s, C5), 6.73 (2H, d, J=9.2Hz), 7.03-7.15 (9H, m), 7.65 (2H, t, J=8.0Hz), 7.73 (1H, d, J=6.8Hz), 8.05 (2H, d, 9.2Hz), 8.25 (2H, d, J=8.0Hz) (all aromatic H).

^{13}C (DMSO-d_6) (ppm): 18.90 ($OCH_2\mathbf{C}H_3$), 63.15 ($O\mathbf{C}H_2CH_3$), 86.34 (C5), 96.91, 114.99 (C3a, C6a), 115.20, 123.13, 125.41, 126.77, 127.12, 128.01, 128.58, 128.93, 129.91, 133.23, 135.29, 135.84, 139.51, 140.10, 146.80 (all aromatic C), 168.90 (C=O).

Microanalysis, found (theory): C 67.00 (67.28), H 4.79 (4.71), N 12.87 (13.08)

2,6-Diphenyl-3a,6a-di-(4-chlorophenyl)-5-ethylcarbonyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9d). 21% yield of a yellow solid. M.p. 181-182°C

IR (KBr) (cm^{-1}): 1741, 1598, 1492, 1468, 1305, 1236, 1092, 832, 746, 685.

^1H (DMSO-d_6) (ppm): 1.35 (3H, t, J=6.8Hz, $OCH_2C\mathbf{H_3}$), 4.37-4.48 (2H, m, $OC\mathbf{H_2}CH_3$), 5.68 (1H, s, C5), 6.61 (2H, d, J=8.8Hz), 6.80 (1H, t, J=7.2Hz), 7.11-7.16 (4H, m), 7.23-7.26 (4H, m), 7.48 (2H, d, J=7.6Hz), 7.64 (2H, t, J=8.0Hz), 7.73 (1H, t, J=6.8Hz), 8.22 (2H, d, J=7.6Hz) (all aromatic H).

^{13}C (DMSO-d_6) (ppm): 14.29 ($OCH_2\mathbf{C}H_3$), 62.81 ($O\mathbf{C}H_2CH_3$), 86.97 (C5), 96.73, 114.35 (C3a, C6a), 115.89, 120.28, 123.11, 128.12, 128.58, 128.88, 129.20, 129.87, 133.16, 133.28, 133.71, 135.09, 136.29, 140.12, 140.94 (all aromatic C), 169.83 (C=O).

Microanalysis, found (theory): C 64.35 (64.41), H 4.44 (4.32), N 9.76 (10.01)

2-Phenyl-3a,6a-di-(4-chlorophenyl)-6-(4-nitrophenyl)-5-ethylcarbonyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9e). 26% yield of a yellow solid. M.p. 178-180°C

IR (KBr) (cm^{-1}): 1747, 1600, 1466, 1509, 1326, 1173, 1137, 1115, 1094, 752, 690.

^1H (DMSO-d_6) (ppm): 1.39 (3H, t, J=6.8Hz, $OCH_2C\mathbf{H_3}$), 4.46-4.50 (2H, m, $OC\mathbf{H_2}CH_3$), 5.98 (1H, s, C5), 6.71 (2H, d, J=9.2Hz), 7.08-7.15 (4H, m), 7.25-7.30 (4H, m), 7.65 (2H, t, J=8.0Hz), 7.74 (1H, t, J=7.2Hz), 8.09 (2H, d, J=9.6Hz), 8.24 (2H, d, J=7.6Hz) (all aromatic H).

^{13}C (DMSO-d_6) (ppm): 14.29 ($OCH_2\mathbf{C}H_3$), 62.79 ($O\mathbf{C}H_2CH_3$), 86.97 (C5), 96.74, 114.36 (C3a, C6a), 115.89, 120.25, 123.12, 128.11, 128.58, 128.89, 129.19, 129.85, 133.14, 133.27, 133.70, 135.11, 136.30, 140.13, 140.95 (all aromatic C), 169.83 (C=O).
Microanalysis, found (theory): C 59.72 (59.60), H 4.05 (3.84), N 11.12 (11.59)
2,3a,6,6a-Tetraphenyl-5-trichloromethyl-3,3a,5,6-tetrahydro-oxazolo-[5,4-d]-1,2,3-triazole (9g). 46% yield of an off-white solid. M.p. 163-164^{o}C
IR (KBr) (cm^{-1}): 1589, 1487, 1461, 767, 697.
^{1}H (DMSO-d_6) (ppm): 6.28 (1H, s, C5-H), 7.05-7.28 (13H, m), 7.50 (2H, d, J=8Hz), 7.68 (2H, d, J=8Hz), 7.76 (1H, t, J=8Hz), 8.24 (2H, d, J=8Hz), (all aromatic H).
^{13}C (DMSO-d_6) (ppm): 97.15 (C5), 102.04, 102.30 (C3a, C6a), 112.50, 124.09, 127.87, 128.63, 128.77, 129.32, 129.55, 130.11, 130.74, 133.86, 137.87, 138.74, 141.35, 144.28 (all aromatic C).
Microanalysis found (theory):C 62.58 (62.76), H 3.93 (3.95), N 10.34 (10.46)

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References

1. Byrne, C.; Draper, S.M.; James, J.P.; Long, C. *J. Chem. Res*. **1995**, 2501.
2. (a) Angadiyavar, C.S.; Sukumaran, K.B.; George, M.V. *Tetrahedron Lett.* **1971**, 633. (b) Sukumaran, K.B.; Angadiyavar, C.S.; George, M.V. *Tetrahedron* **1972**, *28*, 3987. (c) Butler, R.N.; Cunningham, D.; James, J.P.; McArdle, P. *J. Chem. Soc., Chem. Commun.* **1983**, 762.
3. (a) Butler, R.N.; Colleran, D.M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2159. (b) Butler, R.N.; Grogan, D.C.; McDonald, P.D.; Burke, L.A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3587.
4. (a) Albrecht, R.; Kresze, G. *Chem. Ber*. **1964**, *12*, 949. (b) Boger, D.L.; Weinreb, S.N. *Hetero Diels-Alder Methodology in Organic Synthesis*, Academic: San Diego, 1987. (c) Boger, D.L.; Kasper, A.m. *J. Am. Chem. Soc*. **1989**, *111*, 1517. (d) Boger, D.L.; Corbett, W.L.; Curran, T.T.; Kasper, A.M. *J. Am. Chem. Soc*. **1991**, *113*, 1713.
5. Sisko, J.; Weinreb, S.M. *J. Org. Chem*. **1990**, *55*, 393.
6. (a) Tschaen, D.M.; Turos, E.; Weinreb, S.M. *J. Org. Chem*. **1984**, *49*, 5058. (b) Melnick, M.J.; Freyer, A.J.; Weinreb, S.M. *Tetrahedron Lett*. **1988**, *29*, 3891.
7. Davis, F.A.; Reddy, R.T.; Reddy, R.E. *J. Org. Chem*. **1992**, *57*, 6387.
8. Kresze, G.; Wucherpfennig, W. *Angew. Chem., Int. Ed.* **1967**, *6*, 149.
9. Butler, R.N.; O'Shea, D.F. *J. Chem. Soc. Perkin Trans 1* **1994**, 2797.
10. (a) Sukumaran, K.B.; Satish, S.; George, M.V. *Tetrahedron* **1974**, *30*, 445. (b) Alexandrou, N.E. *Tetrahedron* **1966**, *22*, 1309.

11. (a) Albrecht, R.; Kresze, G.; Mlakar, B. *Chem. Ber.* **1965**, *98*, 1431. (b) Baillargé, M.; Le Goffic, F. *Synth. Commun.* **1987**, *17*, 1603. (c) Love, B.E.; Raje, P.S.; Williams, T.C. *Synlett* **1994**, 493.

