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On the reaction of diphenylketene with isocyanides

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The products obtained from the reaction of diphenylketene with a variety of isocyanides are shown to depend heavily on the concentration of diphenylketene; a high concentration results in the precedented dioxolane derivatives, at much lower concentrations the reactions follow an alternative course and polycyclic β-lactams are generated by a cascade of formal pericyclic reactions.

Introduction

The reaction of aryl and diaryl ketenes with isocyanides, to afford adducts comprising a 2 : 1 ketene : isocyanide stoichiometry, has been known for more than 40 years.[1] A structure (**2**) was proposed for these adducts based on analysis of the products formed from their successive treatment with concentrated hydrochloric acid and sodium methoxide, in combination with IR data; this 4-iminocyclopenta-1,3-dione structure may be envisaged to form by sequential *C*-alkylations of enolate-type intermediates (Scheme 1). Sixteen years later, with the benefit of ^{13}C NMR data, the Ugi group revised the original assignment to an isomeric 2,5-dialkylidene-4-imino-1,3-dioxolane structure (**3**)[2] formed by sequential *O*-alkylations.

In the intervening period, Gambarayan had assigned structure **4** (Fig. 1) to the major products formed in the reactions of bis(trifluoromethyl)ketene with representative isocyanides;[3] subsequently Moore reported the 'unusual' products (**5**) of isocyanides with *tert*-butylcyanoketene, these products being, in fact, dioxolanes analogous to those described by Gambarayan, and by Ugi in his revision.[4]

In mechanistically related work, Hoffmann reported the reaction of dimethoxycarbene with diphenylketene to afford dioxolane **6** (Fig. 1).[5] Contemporaneous with these discoveries, Mukaiyama described[6] the formation of an unidentified 2 : 1 adduct of diphenylketene and triethylphosphite, the structure of which was solved eight years later by Baldwin who showed it to be the 1,3,2-dioxaphospholane derivative **7**, similar to Ugi's isocyanide adducts.[7] This process proved to have some generality.[8] In a separate study, having a degree of symmetry with the phosphorus(III) chemistry, Taylor's group noted that the reaction of nitrone **8** with dimethylketene formed two (major) unidentified compounds in addition to the (minor) expected products;[9] in this case, ten years elapsed before the major pathway was shown to involve an isocyanide/ketene interaction resulting in compound **9** and its hydrolysis product.[10]

The mechanism of these formal [2 + 2 + 1] cycloadditions has not been fully established but, in the isocyanide case, the presumed intermediacy of zwitterion **1**, formally an imine-substituted oxyallyl, suggested to us the possibility of engineering conditions in which this adduct might be trapped with 1,3-dienes to result in α-iminocycloheptenones (**10**, Scheme 2), a reaction that might have some utility in synthesis, particularly if the diene could be tethered in some way to the zwitterion.[11] Whilst this proposal proved fanciful,[12] during the course of this study we discovered a new pathway in the ketene/isocyanide manifold and, as a bonus, were able to obtain the first X-ray crystallographic confirmation of the structures of compounds of general structure **3**.

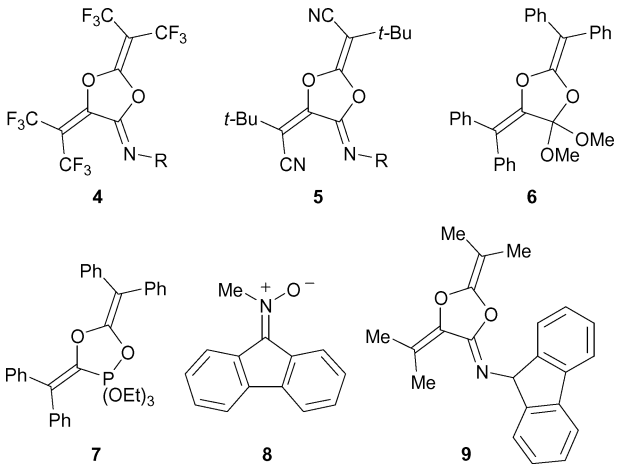
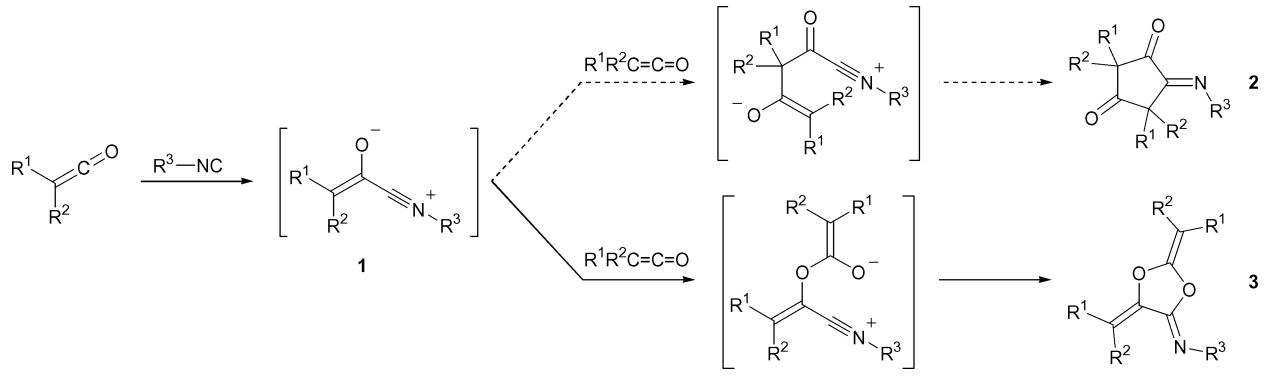


Fig. 1



Scheme 1 The reaction of isocyanides with ketenes as first formulated (dashed arrows) and as later modified (solid arrows).

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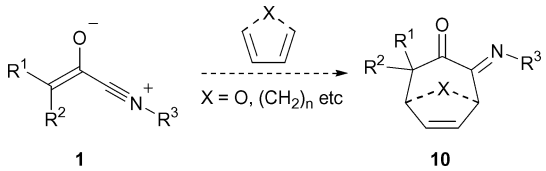


1 10

Scheme 2 Proposed trapping of the isocyanide + ketene adduct by cycloaddition.

Results and discussion

Addition of isocyanides **11**–**14** to a stirred solution of diphenylketene, in dichloromethane, ether, or acetonitrile, in the presence of an excess of isoprene as a potential trapping diene, gave rise to the normal 2 : 1 ketene/isocyanide adducts **15**–**18** respectively (Fig. 2) with no apparent involvement of the diene. Of these adducts, only the *tert*-butyl derivative (**16**)[2] had been reported but the benzyl derivative (**17**) is the correct structure for the compound (*cf.* **2**) misassigned in Ugi's 1961 paper. The ^{1}H and ^{13}C NMR spectra of these compounds indicate the formation of a predominant or single diastereomer about the imine double bond; this was supported in three of the four cases by X-ray diffraction studies of crystals grown by layered diffusion of either methanol or ethanol into di- or tetrachloromethane, and their structures are confirmed as the dioxolanes (Fig. 3).†

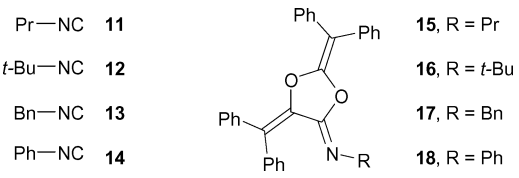


Fig. 2

Clearly, under these conditions, the added diene is unable to compete effectively with excess diphenylketene for zwitterion **1** ($R^1 = R^2 = Ph$). In a first attempt to lower the effective concentration of the ketene and therefore bias the reaction towards cycloaddition, diphenylketene (2.0 equiv.) was added over 8 h by syringe pump to a solution of isocyanide **11** and isoprene (5.0 equiv.) in dichloromethane at 20 °C. In this case the major product was found not to be the Ugi-type 2 : 1 adduct but a 3 : 1 adduct in 40% yield, this yield remaining essentially unchanged when the reaction was repeated in the absence of isoprene. Characterisation of this material proved to be difficult on the basis of spectroscopic data alone, but an absorption at 1755 cm^{-1} in the IR spectrum and a pair of diastereotopic CH_2N protons in the ^{1}H NMR spectrum [2.68 (1 H, ddd, *J* 14.0, 8.3, 6.3), 3.06 (1 H, ddd, *J* 14.0, 8.4, 7.5)] suggested the presence of a β-lactam which, mechanistically, was expected to arise from formal [2 + 2] cycloaddition of the ketene to an intermediate imine. On the basis of these data structure **21** was proposed which we envisaged to arise *via* electrocyclisation of the reactive zwitterion, in the absence of a high concentration of diphenylketene, tautomerisation, and successive [2 + 2][14] and ene reactions to bring the molecule to a kinetically stable state (Scheme 3). Once more, X-ray crystallography was able to confirm the prediction (Fig. 4). In an attempt to activate the zwitterion, by trapping the nominal enolate to generate a reactive extended nitrilium ion,[15] the reaction was repeated in the presence of TMSCl (5.0 equiv.). Although this modification was ineffective in bringing about reaction with the isoprene, it did suppress the ene reaction and two diastereomers of the 'interrupted cascade' products **19** and **20** (2.6 : 1 ratio, Scheme 3) were obtained, the minor isomer (**20**) crystallising from methanol to allow X-ray analysis (Fig. 4).

† CCDC reference numbers 283680–283684. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b512826a

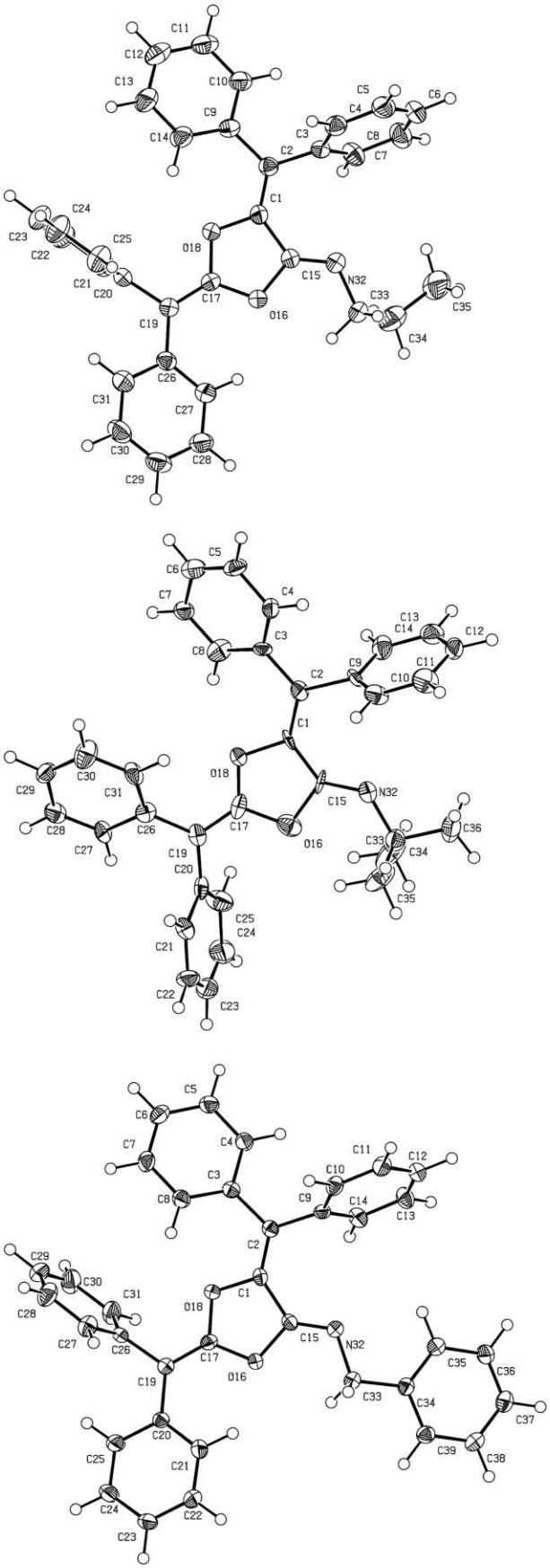
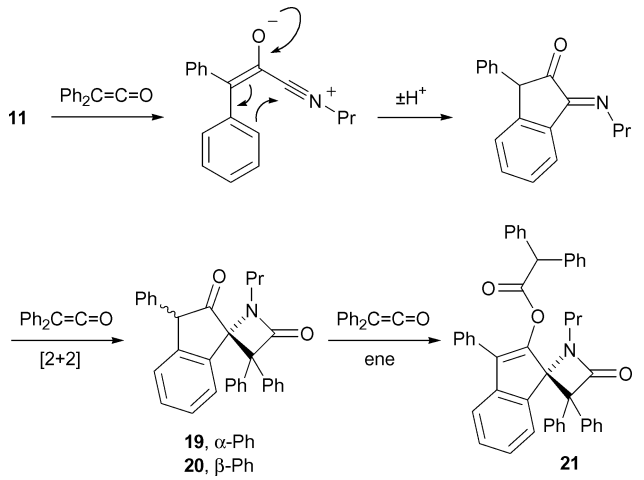


Fig. 3 ORTEP representations of isocyanide/ketene adducts **15**–**17**.[13]

In a final attempt to push the reaction in the desired direction, three diene-tethered isocyanides **24**, **26**, and **27** were prepared by the straightforward routes summarised in Scheme 4.[17] Amongst their more obvious attributes, a characteristic feature of these isocyanides is the splitting, by coupling to ^{14}N ($I = 1$), of ^{1}H



Scheme 3 Reaction cascade when diphenylketene is added slowly to propylisocyanide (**11**).

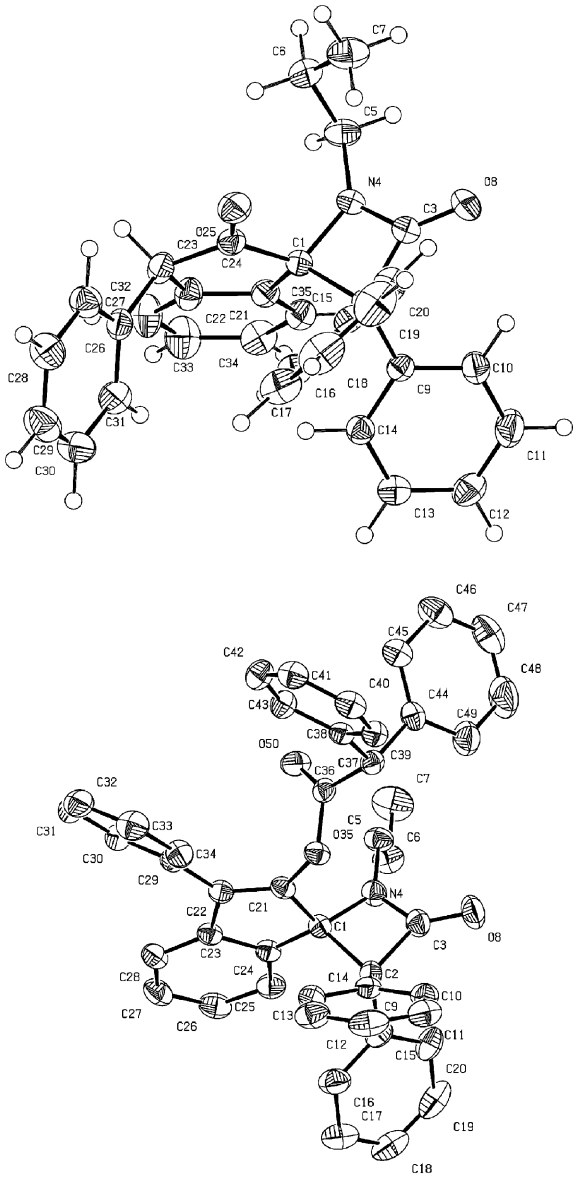
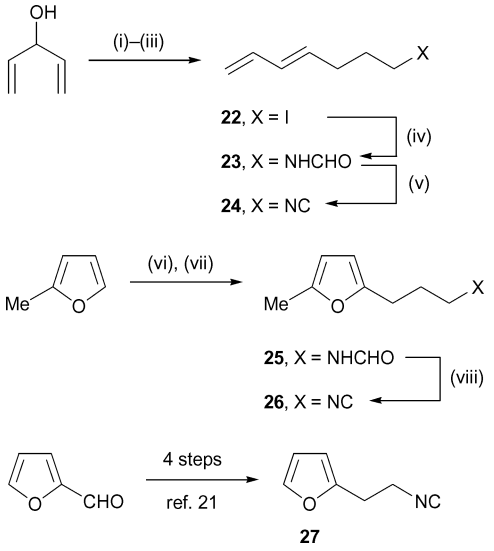


Fig. 4 ORTEP representations of novel isocyanide/ketene adducts **20** and **21** (some hydrogens omitted for clarity).[16]

and ^{13}C NMR resonances of nuclei in close proximity to the isocyanide nitrogen.[18] When acyclic diene **24** and cyclic diene **26**, both carrying three-carbon tethers to the isocyanide functionality, were subjected to the standard conditions, complex product mixtures formed from which only the respective 3 : 1 adducts **28** and **29** (Fig. 5) could be isolated, in low yield. Interestingly, the two-carbon tethered diene (**27**) entered into a cleaner reaction to produce the spirocyclic indanones **30** and **31** (3.5 : 1 ratio) in moderate yield; why the ene reaction was suppressed in this reaction remains unclear to us.



Scheme 4 Reagents and conditions: (i) $CH_3C(OEt)_3$, $EtCO_2H$, reflux, 18 h (65%); (ii) $LiAlH_4$, THF, 0 °C → 20 °C, 18 h (78%); (iii) I_2, PPh_3, imidazole, CH_3CN, 20 °C, 4 h (91%); (iv) $NaN(CHO)_2$, DMF, 100 °C, 48 h then KOH, EtOH, 20 °C, 2 h (75%); (v) $POCl_3$, Et_3N, THF, 0–5 °C, 2 h (75%); (vi) BuLi then 1-bromo-3-chloropropane, −78 °C → 20 °C, 18 h (76%); (vii) as (iv) but with added NaI in the substitution step (79%); (viii) as (v) for 1 h (71%).

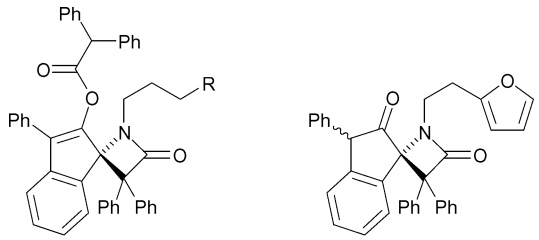


Fig. 5 β-Lactam products formed with tethered dienes.

Conclusion

We have shown in this work that zwitterions of general structure **1** enter into formal electrocyclisation reactions in addition to their known trapping on oxygen by ketenes. With suitably functionalised substituents ($R^{1–3}$) and appropriate choice of reaction conditions, it is conceivable that new complexity-generating transformations of these interesting intermediates will be discovered that lead to novel molecular frameworks in a single reaction step from simple precursors.

Experimental

Diphenylketene,[19] propyl-,[20] benzyl-,[20] and phenylisocyanide,[20] sodium diformylimide,[17] 2-(3-chloropropyl)-5-methylfuran,[17] and isocyanide **27**[21] were prepared according to literature procedures; all other reagents and solvents were obtained commercially and purified before use by standard procedures.

(*Z*)-4-Propylimino-2,5-bis(diphenylmethylene)-1,3-dioxolane (15)

To a stirred solution of diphenylketene (1.94 g, 10.0 mmol) in ether (10 mL) at −20 °C was added propylisocyanide (0.4 mL, 5.0 mmol) in one portion *via* syringe. The mixture

was stirred for 1 h at −20 °C and allowed to warm up to RT over 12 h. Concentration of the mixture *in vacuo* gave a solid residue that was purified by column chromatography (silica, 20 : 1 petrol : ether) to give the title compound (**15**) as yellow needles (1.63 g, 71%). Mp 115–118 °C; R_f 0.58 (2 : 1 petrol : ether); ν_{max} (KBr)/cm^{-1} 3053 w, 2928 w, 1719 m, 1666 s, 1628 m, 1495 w, 1443 m, 1384 w, 1216 s, 1184 s, 1066 m, 1006 s, 761 m, 700 s; δ_H (400 MHz, $CDCl_3$) 0.74 (3 H, t, *J* 7.4, CH_3), 1.35 (2 H, m, CH_2CH$_3$), 3.27 (2 H, *J* 6.3, CH_2N), 7.18–7.31 (20 H, m, 4 × Ph); δ_C (100.6 MHz, $CDCl_3$) 11.8, 23.5, 50.2, 92.6, 122.1, 126.1, 126.4, 127.8, 127.9, 128.0, 128.1, 128.6, 129.6, 129.8, 130.1 (two peaks), 130.9, 134.6, 136.0, 136.8, 137.0, 137.5, 144.1, 150.9; *m*/*z* (APCI+) 458 (MH$^+$, 100%); found: C 83.76, H 6.04, N 3.07; $C_{32}H_{27}NO_2$ requires: C 84.00, H 5.95, N 3.06.

(*Z*)-4-*tert*-Butylimino-2,5-bis(diphenylmethylene)-1,3-dioxolane (16)[2]

Diphenylketene (0.78 g, 4.02 mmol), as a solution in dichloromethane (10 mL), was added in one portion to a solution of *tert*-butylisocyanide (0.21 mL, 2.0 mmol) in dichloromethane (50 mL) and the mixture was stirred for 16 h at RT. Concentration of the mixture *in vacuo* gave a yellow solid that was purified by column chromatography (silica, 20 : 1 petrol : ether) to give the title compound (**16**) as yellow needles (0.55 g, 58%). Mp 164 °C (lit.[2] mp 167–169 °C); R_f 0.64 (2 : 1 petrol : ether); ν_{max} (KBr)/cm^{-1} 3056 w, 2968 m, 1728 m, 1668 s, 1636 s, 1599 m, 1495 m, 1444 s, 1253 s, 1221 s, 1187 s, 1042 m, 1006 s, 988 s, 817 m, 766 s, 697 s, 616 m, 584 m; δ_H (200 MHz, $CDCl_3$) 1.16 (9 H, s, *t*-Bu), 7.31–7.54 (20 H, m, 4 × Ph); δ_C (50.3 MHz, $CDCl_3$) 29.7, 55.0, 92.5, 121.9, 126.3, 127.5, 127.7, 127.9, 128.0, 128.1 (two peaks), 129.8, 129.9 (two peaks), 131.0, 135.6, 136.4, 137.0, 137.3, 137.8, 139.3, 151.3; *m*/*z* (APCI+) 472 (MH$^+$, 58%), 416 (100), 222 (41); accurate mass: found: 472.2272; $C_{33}H_{30}NO_2$ (MH$^+$) requires 472.2276.

(*Z*)-4-Benzylimino-2,5-bis(diphenylmethylene)-1,3-dioxolane (17)

To a stirred solution of diphenylketene (388 mg, 2.0 mmol) in ether (10 mL) was added benzylisocyanide (0.12 mL, 1.0 mmol) in one portion *via* syringe and the mixture was stirred at RT for 16 h. Concentration of the mixture *in vacuo* gave a yellow solid that was purified by column chromatography (silica, 10 : 1 petrol : ether) to give the title compound (**17**) as yellow needles (0.33 g, 65%). R_f (0.63 2 : 1 petrol : ether); mp 146 °C (lit.[1] for the misassigned cyclopentyl structure, mp 150–151 °C); ν_{max} (KBr) 3059 w, 3029 w, 1720 s, 1665 s, 1632 s, 1598 s, 1495 s, 1444 s, 1358 m, 1247 s, 1219 s, 1186 s, 1023 s, 990 s, 819 m, 724 s, 629 s; δ_H (400 MHz, $CDCl_3$) 4.54 (2 H, s, PhCH_2), 6.99 (2 H, d, *J* 8.0) and 7.14–7.43 (23 H, m, 5 × Ph); δ_C (100.6 MHz, $CDCl_3$) 51.7, 126.4 (two peaks), 126.5, 127.1, 127.8, 127.9, 128.0, 128.1, 128.2 (two peaks), 129.7, 129.8, 130.0, 130.9, 136.2, 136.7, 136.9, 137.3 this spectrum was too weak for some of the 4° carbons to be resolved; *m*/*z* (APCI+) 506 (MH$^+$, 100%); accurate mass: found: 506.2126; $C_{36}H_{28}NO_2$ (MH$^+$) requires 506.2120.

(*Z*)-4-Phenylimino-2,5-bis(diphenylmethylene)-1,3-dioxolane (18)

To a stirred solution of diphenylketene (0.78 g, 4.02 mmol) in dichloromethane (10 mL) was added phenylisocyanide (0.21 g, 2.04 mmol) in one portion *via* syringe and the mixture was stirred at RT for 16 h. Concentration of the mixture *in vacuo* gave a yellow solid that was recrystallised from chloroform/methanol to give the title compound (**18**) as yellow needles (0.77 g, 78%). Mp 204–206 °C; ν_{max} (KBr)/cm^{-1} 3052 w, 1716 m, 1672 s, 1672 m, 1588 w, 1487 m, 1443 m, 1258 s, 1214 s, 1183 s, 1171 s, 1005 s, 758 m, 690 s; δ_H (400 MHz, $CDCl_3$) 7.16–7.70 (25 H, m, 5 × Ph); δ_C (100.6 MHz, $CDCl_3$) 93.9, 123.9, 125.1, 126.1, 126.6 (two peaks), 128.0 (two peaks), 128.1, 128.2, 128.3, 128.4, 128.7, 129.9, 130.0 (two peaks), 131.1, 135.7, 136.3, 136.6, 136.8, 137.5, 142.5, 143.3, 151.0; *m*/*z* (APCI +ve) 492 (MH$^+$, 100%); found: C 85.54, H 5.24, N 2.98; $C_{35}H_{25}NO_2$ requires C 85.52, H 5.13, N 2.85.

Spiro[3,3-diphenyl-1-propylazetidin-2-one-4,1′-[2]diphenylacetoxy-[3]phenylindene] (21)

Diphenylketene (0.78 g, 4.02 mmol) dissolved in dry dichloromethane (10 mL) was added over 8 h *via* syringe pump to a solution of propylisocyanide (0.17 mL, 2.0 mmol) in dichloromethane (40 mL). The mixture was stirred for a further 16 h at RT then concentrated *in vacuo*. Purification of the residue by column chromatography (silica, 8 : 1 petrol : ether) gave the title compound (**21**) (348 mg, 40%) as colourless prisms. R_f 0.23 (4 : 1 petrol : ether); mp 182–184 °C; ν_{max} (KBr)/cm^{-1} 3061 w, 2962 w, 1755 s, 1599 m, 1494 s, 1448 s, 1390 m, 1304 m, 1189 w, 1090 s, 1032 w, 900 w, 778 m, 745 s, 700 s, 649 m, 539 w; δ_H (400 MHz, $CDCl_3$) 0.74 (3 H, t, *J* 7.4, CH_3), 1.30–1.40 (2 H, m, CH_2CH$_3$), 2.68 (1 H, ddd, *J* 14.0, 8.3, 6.3, NC*H*H), 3.06 (1 H, ddd, *J* 14.0, 8.4, 7.5, NCH*H*), 4.47 (1 H, s, Ph$_2$C*H*), 6.27 (1 H, d, *J* 7.4), 6.82 (3 H, m), 6.98 (2 H, m), 7.14–7.41 (21 H, m) and 7.73 (2 H, d, *J* 6.8, aromatics); δ_C (100.6 MHz, $CDCl_3$) 11.6, 21.9, 43.4, 56.6, 74.2, 76.0, 120.8, 125.2, 125.9, 126.7–128.9 (many close peaks), 131.5, 132.5, 136.9, 137.0, 139.9, 140.5, 140.7, 148.1, 168.1, 168.9; *m*/*z* (APCI+) 652 (MH$^+$, 40%), 458 (93), 373 (46), 264 (100), 167 (34); found: C 84.66, H 5.68, N 2.20; $C_{46}H_{37}NO_3$ requires C 84.77, H 5.72, N 2.15.

Spiro[3,3-diphenyl-1-propylazetidin-2-one-4,3′-[1]phenylindan[2]one] (19) and (20)

Diphenylketene (0.44 g, 2.27 mmol) was added *via* syringe pump over 18 h, as a solution in dichloromethane (20 mL), to a stirred mixture of propylisocyanide (0.16 mL, 2.2 mmol), isoprene (1.0 mL, 10 mmol) and chlorotrimethylsilane (10.0 mL, 1.0 M in dichloromethane, 10.0 mmol) in dichloromethane (30 mL). On completion of addition, the mixture was allowed to stir for an additional 24 h at RT and concentrated *in vacuo*. Purification by column chromatography (silica, 10 : 1 petrol : ether) afforded an inseparable mixture of the title compounds (**19** and **20** in a 2.6 : 1 ratio), a waxy solid (137 mg, 27%). R_f 0.31 (4 : 1 petrol : ether); ν_{max} (KBr)/cm^{-1} 3060 w, 2961 w, 2931 w, 1755 s, 1494 m, 1448 m, 1390 m, 1304 w, 1090 s, 757 m, 745 m, 700 s; δ_H (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.3, CH_3), 1.36–1.50 (2 H, m, CH_2CH$_3$), 3.01–3.36 (2 H, m, CH_2N), 4.75 (0.72 H, s, PhC*H*CO [in **19**]), 4.80 (0.28 H, s, PhC*H*CO [in **20**]), 6.55–6.65 (1 H, m), 6.72–6.83 (2 H, m), 6.90 (3 H, m), 7.10–7.39 (11 H, m) and 7.50–7.60 (2 H, m, aromatics); δ_C (100.6 MHz, $CDCl_3$) [asterisked resonances are attributable to the minor isomer, **20**] 11.6, 11.7*, 21.7, 21.8*, 42.9, 43.1*, 56.1, 57.2*, 77.3, 78.2, 126.5–130.0 (many close peaks), 135.6, 136.5, 137.1, 137.2, 139.3, 169.2, 209.8; *m*/*z* (APCI+) 458 (MH$^+$, 92%), 264 (100); accurate mass: found: 458.2119; $C_{32}H_{28}NO_2$ (MH$^+$) requires: 458.2120.

N-Hepta-4,6-dienyl formamide (23)

To a stirred solution of 1-iodohepta-4,6-diene (6.0 g, 27 mmol) in DMF (10 mL) was added sodium diformylimide (3.08 g, 32.4 mmol) and the mixture heated at 100 °C for 48 h. The hot reaction mixture was poured into water and allowed to cool. The mixture was extracted with chloroform (3 × 50 mL) and the combined organic phases concentrated *in vacuo*. The residue was dissolved in ethanol (10 mL) and KOH (0.1 g, 1.79 mmol) added. The mixture was stirred for 2 h at RT and concentrated *in vacuo*. Purification by column chromatography (silica, 1 : 2 petrol : ethyl acetate) gave the title compound (**23**) as a colourless oil (2.83 g, 75%). R_f 0.23 (1 : 1 petrol : ethyl acetate); ν_{max} (thin film)/cm^{-1} 3286 s, 3040 s, 2936 s, 2864 s, 1656 s, 1542 s, 1441 s, 1385 s, 1243 s, 1005 s, 953 m, 900 s, 756 w; δ_H (400 MHz, $CDCl_3$) 1.37 (2 H, app. quin, *J* 7.3, CH_2CH$_2$N), 1.88 (2 H, app. q, *J* 7.3, C*H*CH=), 3.08 (2 H, app. q, *J* 6.7, CH_2NH), 4.92 (1 H, d,

J 10.1, (*E*)-H7), 5.06 (1 H, d, *J* 17.1, (*Z*)-H7), 5.47 (1 H, dt, *J* 13.1, 6.8, H4), 5.99 (1 H, dd, *J* 13.1, 10.5, H5), 6.26 (1 H, ddd, *J* 17.1, 10.5, 10.1, H6), 6.56 (1 H, br s, N*H*), 8.01 (1 H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$) [major rotamer] 29.5, 30.3, 37.9, 115.5, 132.4, 134.4, 137.8, 161.6; *m/z* (APCI+) 140 (MH^+, 100%), 127 (13), 112 (11); accurate mass: found: 140.1077; $C_8H_{14}NO$ (MH^+) requires: 140.1075.

7-Isocyanohepta-1,3-diene (24)

Phosphorus oxychloride (2.42 mL, 26 mmol) in THF (20 mL) was added dropwise to a stirred solution of amide **23** (3.25 g, 23.3 mmol) and triethylamine (16.3 mL, 117 mmol) in THF (80 mL) keeping the temperature between 0 and 5 °C. The mixture was stirred for a further 2 h at 0 °C and then carefully quenched with water. The organic layer was separated and the aqueous layer extracted with ether (3 × 50 mL). The combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by distillation afforded the title compound (**24**) as a colourless, evil-smelling oil (2.13 g, 75%). Bp 50 °C at 0.1 mmHg; ν_{max} (thin film)/cm^{-1} 2952 s, 2148 s, 1653 m, 1604 m, 1450 s, 1351 m, 1006 s, 954 s, 904 s, 824 w; δ_H (400 MHz, $CDCl_3$) 1.75–1.83 (2 H, m, CH_2CH$_2$N), 2.27 (2 H, app. q, *J* 7.2, CH_2CH=), 3.40 (2 H, tt, *J* 6.7, $^2J_{NH}$ 2.0, CH_2N), 5.03 (1 H, d, *J* 10.0, (*E*)-H1), 5.15 (1 H, d, *J* 16.4, (*Z*)-H1), 5.63 (1 H, dt, *J* 14.8, 7.2, H4), 6.13 (1 H, dd, *J* 14.8, 10.6, H3), 6.31 (1 H, ddd, *J* 16.4, 10.6, 10.0, H2); δ_C (100.6 MHz, $CDCl_3$) 28.4, 28.9, 40.7 (t, $^1J_{NC}$ 6.0), 116.1, 131.9, 132.8, 136.6, 155.9 (t, $^1J_{NC}$ 5.5); *m/z* (APCI+) 122 (MH^+, 100%); accurate mass: found: 122.0971; $C_8H_{12}N$ (MH^+) requires: 122.0969.

***N*-[3-(5-Methylfuran-2-yl)propyl] formamide (25)**

To a stirred solution of 2-(3-chloropropyl)-5-methylfuran (10.0 g, 63.1 mmol) and sodium iodide (21.0 g, 140 mmol) in DMF (80 mL) was added sodium diformylimide (11.4 g, 120 mmol) and the mixture was heated at 100 °C for 48 h. The hot reaction mixture was poured into water and allowed to cool. The mixture was extracted with chloroform (3 × 50 mL) and the combined organic phases concentrated *in vacuo*. The residue was dissolved in ethanol (50 mL) and KOH (0.1 g, 1.79 mmol) added. The mixture was stirred for 2 h at RT and concentrated *in vacuo*. Purification by column chromatography (silica, 1 : 2 petrol : ethyl acetate) gave the amide (**25**) as a colourless oil (9.24 g, 88%). R_f 0.10 (1 : 1 petrol : ethyl acetate); ν_{max} (thin film)/cm^{-1} 3288 s, 3056 m, 2944 s, 1665 s, 1541 s, 1450 s, 1385 s, 1219 s, 1021 s, 783 s; δ_H (200 MHz, $CDCl_3$) 1.83 (2 H, app. quin, *J* 7.0, CH_2CH$_2$NH), 2.22 (3 H, s, CH_3), 2.61 (2 H, t, *J* 7.5, CH_2furan), 3.31 (2 H, app. q, *J* 7.0, CH_2NH), 5.81–5.83 (1 H, m) and 5.86 (1 H, d, *J* 3.0, furan), 6.10 (1 H, br s, NH), 8.13 (1 H, d, *J* 1.5, NHC*H*O); δ_C (50.3 MHz, $CDCl_3$) 13.5, 25.3, 28.0, 37.6, 105.9 (two peaks), 150.5, 153.0, 161.3; *m/z* (APCI+) 168 (MH^+, 100%), 141 (24) 140 (80), 123 (27); accurate mass: found: 168.1029; $C_9H_{14}NO_2$ (MH^+) requires: 168.1025.

2-(3-Isocyanopropyl)-5-methylfuran (26)

Phosphorus oxychloride (4.87 mL, 51.8 mmol) in THF (25 mL) was added dropwise to a stirred solution of amide **25** (7.88 g, 47.1 mmol) and triethylamine (32.8 mL, 0.24 mol) in THF (80 mL) keeping the temperature between 0 and 5 °C. The mixture was stirred for a further 1 h at 0 °C and then carefully quenched with water (20 mL). The organic layer was separated and the aqueous layer extracted with ether (3 × 50 mL). The combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by distillation afforded the isocyanide (**26**) as a colourless, evil-smelling oil (5.0 g, 71%). Bp 108 °C at 0.02 mmHg; ν_{max} (thin film)/cm^{-1} 2957 m, 2925 m, 2149 s, 1570 m, 1450 m, 1287 w, 1219 m, 1020 m, 941 m, 784 s; δ_H (400 MHz, $CDCl_3$) 1.96–2.04 (2 H, m, CH_2CH$_2$NC), 2.26 (3 H, s, CH_3), 2.76 (2 H, t, *J* 7.0, CH_2furan), 3.42 (2 H, tt, *J* 6.4, $^2J_{NH}$ 1.8, CH_2NC), 5.87–5.88 (1 H, m) and 5.93 (1 H, d, *J* 2.8, furan); δ_C (100.6 MHz, $CDCl_3$) 13.5, 24.6, 27.7, 40.7 (t, $^1J_{NC}$ 6.5), 105.9, 106.7, 151.0, 151.5, 156.1 (t, $^1J_{NC}$ 5.5); *m/z* (GCMS, EI+) 149 (M^+, 15%), 95 (100); accurate mass: found: 150.0921; $C_9H_{12}NO$ (MH^+) requires: 150.0919.

Spiro[3,3-diphenyl-1-hepta-4,6-dienylazetidin-2-one-4,1′-[2]diphenylacetoxy[3]phenylindene] (28)

Diphenylketene (0.39 g, 2.01 mmol), as a solution in dichloromethane (10 mL), was added over 24 h *via* syringe pump to a stirred solution of isocyanide **24** (0.24 g, 1.98 mmol) in dichloromethane (300 mL). The mixture was allowed to stir for a further 24 h and concentrated *in vacuo*. Purification by column chromatography (silica, 10 : 1 petrol : ether) afforded the title compound (**28**) as a pale yellow oil (31.1 mg, 7%). R_f 0.22 (4 : 1 petrol : ether); ν_{max} (thin film)/cm^{-1} 2925 w, 1754 s, 1600 w, 1494 m, 1449 m, 1150 m, 1096 s, 1004 m, 746 m, 697 s, 5311; δ_H (400 MHz, C_6D_6) 1.33–1.44 (1 H, m) and 1.45–1.54 (1 H, m, CH_2CH$_2$N), 1.66–1.79 (2 H, m, CH_2CH=), 2.83 (1 H, ddd, *J* 14.4, 8.4, 5.2) and 3.27 (1 H, ddd, *J* 14.4, 8.4, 6.8, CH_2N), 4.65 (1 H, s, C*H*Ph$_2$), 4.89 (1 H, d, *J* 10.2, (*E*)-H7), 5.01 (1 H, d, *J* 16.8, (*Z*)-H7), 5.29 (1 H, dt, *J* 14.7, 7.0, H4), 5.86 (1 H, dd, *J* 14.7, 10.8, H5), 6.19 (1 H, ddd, *J* 16.8, 10.8, 10.2, H6), 6.40 (1 H, d, *J* 7.2), 6.66 (1 H, t, *J* 7.2), 6.87–7.16 (22 H, m), 7.30 (3 H, d, *J* 8.4) and 7.97 (2 H, d, *J* 7.6, aromatics); δ_C (100.6 MHz, $CDCl_3$) 27.9, 30.0, 41.2, 56.6, 74.2, 76.0, 115.1, 120.9, 125.3, 125.9, 126.7–129.0 (complex, many close peaks), 129.9, 130.1, 131.5 (two peaks), 132.4, 132.6, 133.6, 134.9, 136.9 (two peaks), 137.0, 137.1, 137.6, 139.9, 140.4, 140.8, 148.0, 168.1, 168.9; *m/z* (APCI+) 704 (MH^+, 20%), 510 (100), 373 (23), 316 (30), 167 (10); accurate mass: found: 704.3178; $C_{50}H_{42}NO_3$ (MH^+) requires: 704.3165.

Spiro[3,3-diphenyl-1-(3-(5-methylfuran-2-yl)propyl)azetidin-2-one-4,1′-[2]diphenylacetoxy[3]phenylindene] (29)

Diphenylketene (0.39 g, 2.01 mmol), as a solution in dichloromethane (10 mL), was added *via* syringe pump over 24 h to a stirred solution of isocyanide **26** (0.15 g, 0.99 mmol) in dichloromethane (200 mL). The mixture was allowed to stir for a further 24 h and concentrated *in vacuo*. Purification by column chromatography (silica, 4 : 1 petrol : ether) afforded the title compound (**29**) as a colourless oil (50.1 mg, 10%). R_f 0.52 (1:1 petrol : ether); ν_{max} (thin film)/cm^{-1} 3060 w, 2922 w, 1758 s, 1495 w, 1449 m, 1396 m, 1080 w, 1022 w, 737 w, 704 m, 668 w; δ_H (400 MHz, $CDCl_3$) 1.62–1.70 (2 H, m, CH_2CH$_2$N), 2.21 (3 H, s, CH_3), 2.45 (2 H, app. t, *J* 7.8, CH_2furan), 2.74 (1 H, ddd, *J* 14.0, 8.0, 6.4) and 3.17 (1 H, ddd, *J* 14.0, 8.0, 6.4, CH_2N), 4.48 (1 H, s, Ph$_2$C*H*), 5.74 (1 H, d, *J* 2.8) and 5.79–5.80 (1 H, m, furan), 6.27 (1 H, d, *J* 7.2), 6.80–6.87 (3 H, m), 6.93–6.95 (2 H, m), 7.15–7.17 (3 H, m), 7.21–7.39 (18 H, m) and 7.73 (2 H, d, *J* 6.8, aromatics); δ_C (100.6 MHz, $CDCl_3$) 13.5, 25.6, 27.0, 41.2, 56.6, 74.2, 76.0, 105.7, 105.8, 120.8, 125.3, 126.0, 126.7–129.1 (complex, many peaks), 131.5, 132.6, 136.9 (two peaks), 139.9, 140.4, 140.8, 148.0, 150.3, 152.9, 168.1, 168.9; *m/z* (ESI+) 1486 (M_2Na^+, 12%), 754 (MNa^+, 100), 732 (MH^+, 67); accurate mass: found: 732.3105; $C_{51}H_{42}NO_4$ (MH^+) requires: 732.3114.

Spiro[3,3-diphenyl-1-(2-furan-2-ylethyl)azetidin-2-one-4,3′-[1]phenylindan[2]one] (30) and (31)

Diphenylketene (0.87 g, 4.48 mmol) was added *via* syringe pump over 24 h, as a solution in dichloromethane (10 mL), to a stirred solution of isocyanide **27** (180 mg, 1.49 mmol) in dichloromethane (100 mL). On completion of addition the mixture was allowed to stir for an additional 24 h at RT and concentrated *in vacuo*. Purification by column chromatography (silica, 3 : 1 petrol : ether) afforded the title compounds (**30**) and (**31**) as an inseparable mixture of diastereomers (ratio, 3.5 : 1), a viscous oil (280 mg, 37%). R_f 0.27 (4 : 1 petrol : ether); ν_{max}

(thin film)/cm^{-1} 3057 w, 2928 w, 1759 s, 1495 m, 1449 m, 1395 m, 1078 w, 735 m, 701 m; δ_H (400 MHz, $CDCl_3$) 2.77–2.86 (1 H, m) and 2.90–3.10 (1 H, m, C*H*$_2$furan), 3.28–3.40 (1 H, m) and 3.45–3.65 (1 H, m, CH_2N), 4.76 (0.22 H, s, PhC*H* [in **31**]), 4.78 (0.78 H, s, PhC*H* [in **30**]), 6.05 (0.22 H, d, *J* 3.2, furan [in **31**]), 6.12 (0.78 H, d, *J* 3.0, furan [in **30**]), 6.25 (0.22 H, dd, *J* 3.2, 1.6, furan [in **31**]), 6.29 (0.78 H, dd, *J* 3.0, 2.0, furan [in **30**]), 6.39 (1 H, d, *J* 8.0), 6.77–7.34 (17 H, m) and 7.51 (2 H, app. d, *J* 6.4, aromatics); δ_C (100.6 MHz, $CDCl_3$) [asterisked peaks are attributable to the minor isomer, **31**; some of the 4° carbon resonances are unassignable to **30** or **31**] 27.1, 39.5*, 40.0, 56.0*, 57.2, 77.5, 78.4, 106.5, 110.2, 125.8, 126.5, 126.8–129.2 (many peaks), 130.1, 130.2, 135.5, 135.9, 136.3, 136.6, 136.8, 136.9, 137.0, 139.3, 141.1, 141.4, 152.1 (two peaks), 169.2, 169.3*, 209.7*, 210.4; *m*/*z* (ESI+) 1041 (M_2Na^+, 21%), 647 (62), 532 (MNa^+, 47), 510 (MH^+, 100); accurate mass: found: 510.2066; $C_{35}H_{28}NO_3$ (MH^+) requires: 510.2069.

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