The Synthesis of Novel *N*-Heterocycles from 2-Azido-, 2-Vinylazido- and 2-Formyl-1,6-Methano[10]annulene-2-carbaldehydes

Hans Suschitzky,*[a] Walter Kramer,[b] Richard Neidlein,*[b] Peter Rosyk[b] and Thomas Bohn[b] (in Part)

[a] *The Ramage Laboratories, Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, UK*

[b] *Pharmazeutisch-Chemisches Institut der Universität Heidelberg, Im Neuenheimer Feld 364, D-6900 Heidelberg, Germany*

The preparation of 2-azido-1,6-methano[10]annulene **2** from 2-lithioannulene is described. The annulene **2** underwent ring expansion on thermolysis in the presence of various secondary amines to give novel bridged aza-annulenes of type **3** and also gave 1,3-dipolar addition products. When heated the vinyl azides **13** ($R^1 = R^2 = H$) and **13** [$R^1 = H$, $R^2 = CH{=}C(CO_2Et)N_3$] underwent cyclisation to give the annuleno[3,2-*b*]pyrroles **14** and **15** respectively. Annulenopyridines such as **18** were obtained from the iminophosphorane **16** *via* an aza-Wittig reaction with phenyl or allyl isothiocyanate or tolyl isocyanate. Some 2-formyl derivatives **1** ($R^1 = CHO$) when treated with tosylmethyl isocyanide yielded oxazolylannulenes **19**.

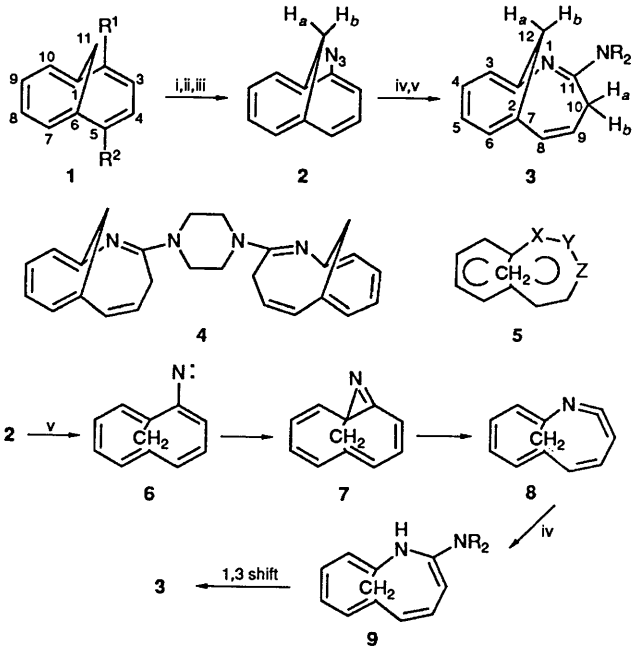
Aryl azides are versatile precursors for the synthesis of *N*-heterocycles commonly by ring expansion,[1] 1,3-cycloaddition,[2] and intramolecular annelation.[1] In continuation of our interest in this area[3] we now describe the preparation and some reactions of azides derived from [10]annulene **1** ($R^1 = R^2 = H$). The conventional route to the azide **2** from the required amine by diazotisation followed by addition of sodium azide was not feasible because of the instability and enaminic character of the amine[4] **1** ($R^1 = NH_2$, $R^2 = H$). The azide **2** was best made by modifying an alternative route,[5] namely from the 2-bromo compound[6] **1** ($R^1 = Br$, $R^2 = H$) by treatment with butyllithium followed by quenching with tosyl azide. The resulting triazene was hydrolysed, as an ethereal suspension, with sodium pyrophosphate to give the azide **2**, after chromatography, in *ca.* 30% yield. Owing to its instability to air and light it was characterised by conversion into its iminophosphorane **1** ($R^1 = N{=}CPh_3$, $R^2 = H$). When the azide **2** was heated in THF (tetrahydrofuran) in the presence of a little TMEDA (tetramethylethylenediamine) as a singlet nitrene stabiliser[1a] and excess of a secondary amine, *e.g.* morpholine, it underwent ring expansion to give 11-morpholino-10*H*-2,7-methanoaza[11]annulene **3** (NR_2 = morpholino) in 60% yield. The compound is temperature and light sensitive turning into an intractable tar unless kept in a refrigerator. Slow decomposition of the azide **2** in THF (tetrahydrofuran) at room temperature takes up to 14 d and gives a cleaner product **3** (NR_2 = morpholino). With piperazine as the secondary amine the *N*,*N*′-diaza[11]annulenyl)piperazine **4** is obtained and products derived from other secondary amines are listed in Table 1. Since only one type of aza[11]annulene **3** is formed the intramolecular attack of the electrophilic nitrene **6** occurs at C-1 of the annulene **6** ⟶ **7**. This selectivity can be ascribed to the inductive effect of the methano group which renders the bridgehead carbon C-1 more nucleophilic than C-10. It is noteworthy that intermolecular insertion of a nitrene (generated thermally from methoxycarbonyl azide) was recently reported[7] to occur at similar rates at all positions of the annulene **1** ($R^1 = R^2 = H$) yielding the three methanoaza-[11]annulenes in comparable, albeit, low yield (*ca.* 5%) **5** (X, Y or Z = NCO_2Me, the remaining positions then being CH). The steps leading to the ring enlargement **3** can be visualized as following a mechanism postulated by Chapman[8] for nitrene-induced ring expansions on the basis of argon matrix studies (*cf.* Scheme 1): Formation of the azaundecahexaene **8** by rearrangement of the intermediate azirine **7** is followed by addition of the secondary amine to give **9** which by a 1,3-sigmatropic H-shift leads to the observed product **3**. The structural assignment of the new heterocycles **3** was solely based on their ^1H (see Table 1) and ^{13}C NMR spectra, as it has not been possible so far to grow suitable crystals for an X-ray study. The broken ring current in these aza[11]annulenes **3** is reflected in a slight upfield shift of the vinylic protons (δ 5.6–6.9) compared to the δ_{CH} positions of the starting annulene **1** ($R^1 = R^2 = H$; δ_{CHs} centred at 7.1). The bridge protons (12-H) are no longer shielded and are found downfield at δ 1.49 and 2.75 in contrast to the [10]annulene bridge **1** [$R^1 = R^2 = H$, $\delta(CH_2)$ at -0.5]. The geminal proton H*a* at C(10) on being irradiated produced an NOE in the α-methylene protons of the morpholine as well as in 9-H. The identity of 8-H followed from a NOE observed in 8-H and 6-H on irradiation of 6-H. The protons 5- and 4-H are recognisable from their doublet of doublet structure while 8-, 6- and 3-H appear as simple doublets which are only slightly broadened owing to a non-resolved coupling influence by other protons. The position of the *N*-heteroatom is established by irradiating 3-H leading only to a NOE in 4-H which at the same time assigns the position of 5-H. The relative conformation of the two methylenes at positions 10 and 12 was found to be pseudo-chair (*trans*) because irradiation of 12*b*-H does not elicit a NOE response in any of the 10-H protons, as would be expected from a pseudo-boat *cis*-orientation. A small NOE was moreover observable in 8-H which according to a model (Dreiding) is nearer to 12*b*-H than in a *cis*-arrangement. Further structural information emerges from the ^{13}C NMR spectrum. The bridgehead atoms C-7 and C-2 appear at 122.2 and 136.6 ppm respectively. This difference of *ca.* 14 ppm is undoubtedly due to the proximity of one of the carbons (C-2) to the N-atom. The upfield shift of C-3 to 109.9 ppm is borne out by this view as it can be regarded as an enamine C-atom. NMR data of the other aza[11]annulenes prepared from the azide **2** are so similar that they are omitted from Table 1 except for the respective amino substituent.

The azide **2** could also be made to react in the dark at ambient temperature with some dipolarophiles. With dimethyl acetylenedicarboxylate (DMAD) the expected triazole **10** ($R^1 = R^2 = CO_2Me$) was obtained. The unsymmetrical methyl propiolate gave an inseparable mixture of triazoles **10** ($R^1 =$

Table 1 10-Aza[11]annulenes **3** from pyrolysis of the azide **2** and secondary amines

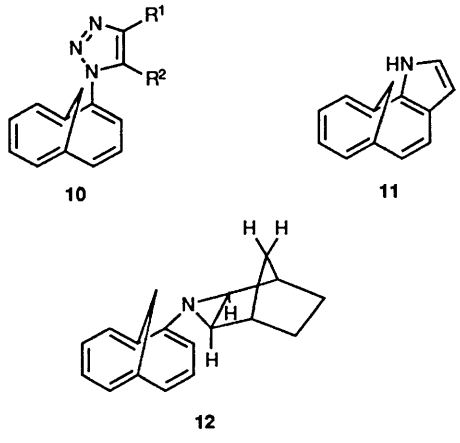
Compound **3** NR_2	Yield (%)	M.p. (°C)	Found (%) (Required) C	H	N	Formula	δ($CDCl_3$; 250 MHz)[b]
Morpholino	60	71	74.2 (74.4)	7.5 (7.5)	11.4 (11.6)	$C_{15}H_{18}N_2O$	1.49 (1 H, d, *J* 11, 12*b*-H), 2.10 (1 H, dd, *J* 8, J_{gem} 13, 10*b*-H), 2.75 (1 H, d, *J* 11, 12*a*-H), 2.68 (1 H, dd, *J* 8, J_{gem} 13, 10*a*-H), 3.58 (4 H, m, α-CH_2s morpholino), 3.75 (4 H, m, β-CH_2s morpholino), 5.58 (1 H, m, *J* 10, 8-H), 5.88 (1 H, d, *J* 6.5, 3-H), 6.18 (1 H, d, *J* 5.5, 6-H), 6.53 (1 H, dd, *J* 11, 5-H), 6.75 (1 H, dd, *J* 11, 6-H), 6.92 (1 H, d, *J* 10, 4-H)
Diethylamino[a,b]	52	—	—	M^+ 228.3401 (228.3402)		$C_{15}H_{20}N_2$	1.18 (6 H, t, 2 Me), 4.28 (2 H, m, CH_2), 4.50 (2 H, m, CH_2)
Piperidino[a,b]	56	—	—	M^+ 240.1627 (240.1628)		$C_{16}H_{20}N_2$	1.37 (2 H, m, CH_2), 3.48 (4 H, m, $2CH_2$) 3.75 (4 H, m)
N-Methylpiperazinyl[b]	56	86	75.0 (75.3)	8.4 (8.3)	16.2 (16.5)	$C_{16}H_{21}N_3$	2.33 (3 H, s, NMe), 2.44 (4 H, m, $2CH_2$), 3.50 (4 H, m, $2CH_2$)
Compound **4**[b]	42	170	78.7 (78.8)	7.2 (7.1)	14.3 (14.1)	$C_{26}H_{28}N_4$	3.55 (8 H, m, $4CH_2$)

[a] Unstable oil. [b] Proton shifts for the annulene moiety as in the morpholine derivative. *J* values given in Hz.



Scheme 1 *Reagents and conditions:* Buli; ii, Tos–N_3; iii, $Na_4P_2O_7$; iv, R_2NH; heat

CO_2Me, R^2 = H and R^1 = H, R^2 = CO_2Me) with the less hindered isomer **10** (R^1 = CO_2Me, R^2 = H) predominating (2:1). This assignment is based on the ^1H NMR spectrum of the mixture which shows the single triazole proton **10** (R^1 or R^2 = H) of each isomer at δ 8.47 and 8.30 and the methyl group of each isomer **10** (R^1 or R^2 = CO_2Me) at δ 3.97 and 3.77. Irradiation of the proton at δ 8.47 causes enhancement in the aromatic protons of the annulene and irradiation of the methyl group at δ 3.97 affects the single proton at 8.47. On this basis, it is feasible to assign the two above signals to the less hindered isomer **10** (R^1 = CO_2Me, R^2 = H) in which the triazole proton is close enough to the annulene for NOE interaction to occur. The mass spectra of all triazoles prepared **10** (R^1 = R^2 = CO_2Me and R^1 or R^2 = H or CO_2Me) show a fragment *m/z* 181 corresponding to the annelated pyrrole **11**



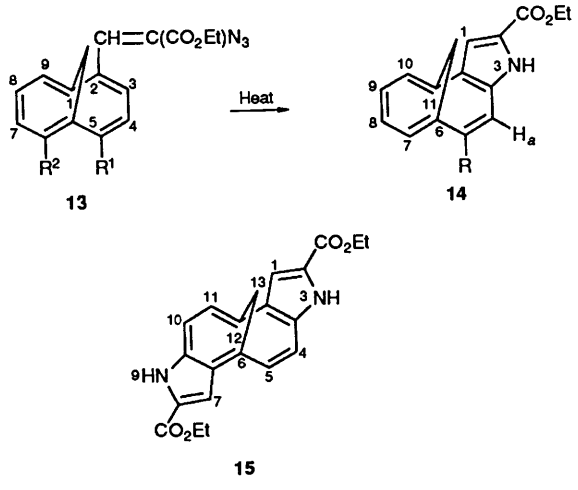
owing to decarboxylation and loss of N_2. This is analogous to the fragmentation pattern observed for naphthalene triazoles.[9] The strained bicycle norbornene which readily undergoes cycloaddition with aryl azides[10] yielded the aziridine **12** when made to react with the azide **2** in toluene at room temperature. It appears that the intermediate triazole is unstable and loses nitrogen to give **12**. As expected, the aziridine proved to be the less hindered *exo*-compound **12**. The geometry follows from the absence of coupling[11] between the *endo*-protons at δ 2.91 and 2.59 with the annulene bridge protons at δ 1.54 and 0.83.

Fused five-membered *N*-heterocycles are conveniently formed from side-chain azides when, on decomposition, the generated nitrene inserts intramolecularly into the requisite C–H bond located four carbon atoms away. For instance, reactions involving the thermolysis of β-azidostyrenes to yield the corresponding indoles are of considerable general interest.[12] We extended this method to the 2-azidoacrylate **13** (R^1 = R^2 = H) prepared from the readily available aldehyde[13] **1** (R^1 = CHO, R^2 = H) by a Knoevenagel condensation with an excess of ethyl azidoacetate in ethanol in the presence of freshly prepared sodium ethoxide. Pyrolysis of the azide **13** (R^1 = R^2 = H) in boiling xylene yielded the pyrrole **14** (R = H) in 97% yield. The intramolecular cyclisation was also successful in a one-pot synthesis starting with 2-*tert*-butoxy-5-formyl compounds[14] **1** (R^1 = CHO, R^2 = OBu^t) to give the

corresponding pyrrole **14** (R = OBu^t). A sharp NH-band at ν = 3300 cm^{-1} and a peak at δ 10.8 (s) as well as a singlet for H*a* at δ 6.54 and presence of the methano-bridge (at δ −0.3 and 1.05; *J* 10 Hz) confirm the structure of **14** (R = OBu^t).

Nitrene insertion involved the 3-position of the [10]annulene and not, as occurred in the ring expansion of the azide **2**, the 1-position. Cyclisation also occurred when the 2,7-bis(azidoacrylate) **13** [R^1 = H, R^2 = CH=C(CO$_2$Et)N$_3$] prepared from 1,6-methano[10]annulene-2,7-dicarbaldehyde and excess of ethyl azidoacetate was thermolysed in boiling *p*-xylene to give the dipyrrolo compound **15** in high yield.

The azidoacrylate **13** (R^1 = R^2 = H) was also utilised to bring about pyrido-annelation by a method recently applied to the synthesis of fused heterocycles[15] such as carbolines and isoquinolines. The iminophosphorane **16** derived from the α-azidoacrylate **13** (R^1 = R^2 = H) by reaction with triphenylphosphine was treated with an isothiocyanate (PhNCS or



13 **14**

15

CH_2=CHCHNCS) or tolyl isocyanate (MeC_6H_4NCO) at room temperature. This was followed by heating under reflux to cause electrocyclic ring-closure to the annulenopyridine **18** (R = Ph, CH_2CH=CH_2, or MeC_6H_4) (*ca.* 70%) *via* the intermediate carbodiimide[15] **17** which was, however, not isolated. As was shown recently for related annelations it is formed by an aza-Wittig reaction between the iminophosphorane **16** and the reagent[15] (*cf.* Scheme 2).

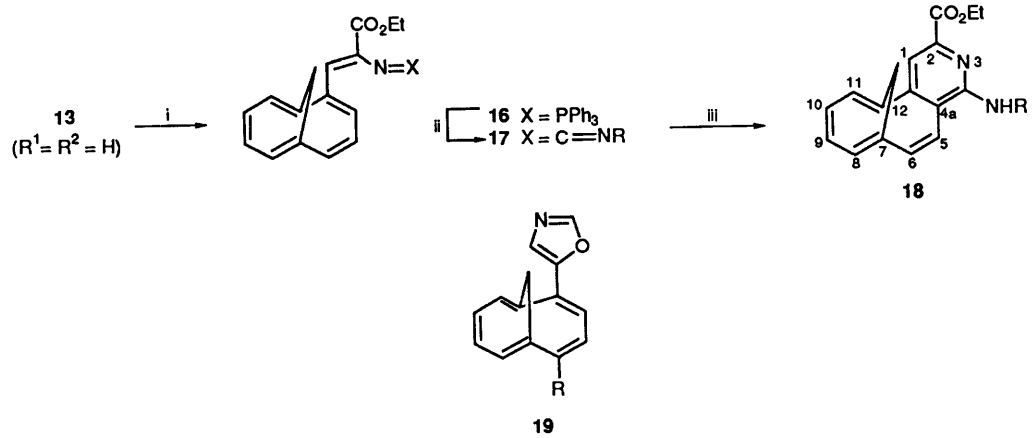
The aldehydes **1** (R^1 = CHO, R^2 = H, OMe or OBu^t) reacted readily with tosylmethyl isocyanide[16] in hot methanol in the presence of potassium carbonate to furnish the corresponding oxazolylannulenes **19** (R = H, OMe or OBu^t).

Experimental

M.p.s were recorded on a Reichert melting-point microscope and are uncorrected. IR spectra were measured on a Perkin-Elmer 325 spectrometer, ^{1}H NMR spectra with a Bruker HX-90E (W.M.-250 MHz) and ^{13}C spectra with a Bruker (62.89 MHz), δ values are given relative to tetramethylsilane (tms). *J* Values are given in Hz. Mass spectra were measured on a Varian MAT 311A spectrometer. For column chromatography silica gel 60 (63–200 μm) (Merck) or neutral alumina 90, grade 1 (63–200 μm) (Woelm) was employed. All solvents were dried by the usual methods.

2-Azido-1,6-methano[10]annulene **2**.—To a solution of 2-bromo-1,6-methano[10]annulene **1** (R^1 = Br, R^2 = H) (12 g, 54 mmol) in freshly distilled, dry diethyl ether (200 cm^3) contained in a 500 cm^3 three-necked flask and kept under argon at −70 °C a solution of butyllithium (2.5 mol dm^{-3}; 23.9 cm^3 60 mmol) was added dropwise. The mixture was stirred for 30 min at −70 °C and then transferred by reverse addition in the dark to a 500 cm^3 flask containing a solution of tosyl azide (11.7 g, 60 mmol) in diethyl ether (100 cm^3). The yellow precipitate of the triazene salt was filtered off, washed repeatedly with cold hexane (4 × 200 cm^3) and then suspended in dry diethyl ether (200 cm^3). Hydrolysis was effected by gradual addition of aqueous (100 cm^3) sodium pyrophosphate (24 g) and by stirring for 2 h at *ca.* 10 °C. The mixture was neutralised with dilute hydrochloric acid and then repeatedly extracted with dichloromethane (6 × 100 cm^3). The combined extracts were evaporated under reduced pressure and the residual brown oil was chromatographed (Al_2O_3, hexane) in the dark to give the *azide* **2** as a yellow oil (3 g, 30%); ν_{max}(KBr)/cm^{-1} 2140 (N_3); δ_H($CDCl_3$; 250 MHz) −0.63 (d, 1 H, 11-H$_a$ *J* 10), −0.25 (d, 1 H, 11-H$_b$ *J* 10), 6.89 (d, 1 H, 3-H, *J* 9.5), 7.03 (dd, 1 H, 4-H, *J* 9), 7.13 (m, 1 H, 8-H or 9-H), 7.28 (m, 1 H, 9-H or 8-H), 7.28 (t, 1 H, 5-H, *J* 9), 7.38 (d, 1 H, 7-H, *J* 8) and 7.69 (d, 1 H, 10-H, *J* 10) (Found: M$^+$, 183.0796. $C_{11}H_9N_3$ requires *M*, 183.0796 (elemental analysis proved unsatisfactory owing to instability of the oil).

2-Triphenylphosphoranylideneamino-1,6-methano[10]annulene **1** (R^1 = NPPh$_3$, R^2 = H).—To a solution of the azide **2** (1 g, 5.5 mmol) in dry diethyl ether (20 cm^3) triphenylphosphine (1.43 g, 5.5 mmol) was added all at once. When the gas evolution had ceased the reaction was agitated for 90 min. The precipitate was filtered off and gave, on recrystallisation (hexane), yellow crystals of the *title compound* **1** (R^1 = NPPh$_3$, R^2 = H) (2.11 g, 92%), m.p. 170 °C; δ_H($CDCl_3$); 250 MHz) −0.74 (d, 1 H, 11-H$_a$, *J* 9.3), 0.22 (d, 1 H, 11-H$_b$, *J* 9.3), 6.15 (d, 1 H, 3-H, *J* 9), 6.50 (d, 1 H, 4-H, *J* 9), 6.76, 7.22 (d, 2 H, 5- and 7-H, *J* 9), 6.97, 7.13 (t, 2 H, 8- and 9-H, *J* 9), 7.96 (d, 1 H, 10-H, *J* 5), 7.35–7.55 (m, 10 H, 2



Scheme 2 *Reagents:* i, PPh_3; ii, PhNCS or CH_2=$CHCH_2NCS$ or MeC_6H_4NCO; iii, Toluene, reflux

Ph) and 7.62–7.74 (m, 5 H, Ph); $\delta_P(CDCl_3)$, 4.22 *m/z* 418 (M^+) (Found: C, 83.55; H, 6.0; N, 3.1. $C_{29}H_{24}NP$ requires C, 83.43; H, 5.79; N, 3.35).

Thermolysis of the Azide **2** *in the Presence of Amines* (cf. *Table* 1).—In a representative procedure, to a solution of the azide **2** (1 g, 5.5 mmol) dissolved in freshly distilled, dry THF (60 cm^3) was added morpholine (5 cm^3, 58.3 mmol) and TMEDA (tetramethylethylenediamine) (5 drops). The reaction mixture was heated under reflux for 3 h in the dark. On cooling, neutral Al_2O_3 was added (15 g) and the solvent and excess of amine were removed under reduced pressure. The residue was chromatographed (Al_2O_3, hexane, followed by hexane–ethyl acetate 10:1) to yield the 11-*morpholino*-10H-2,7-*methano-aza*[11]*annulene* **3** (NR^2 = morpholino) (0.8 g, 60%), m.p. 71 °C; λ_{max}/nm (log ε, MeOH) 235 (4.54) and 290 (4.01); for δ_H and other details *cf.* Table 1. δ_C(62.8 MHz, $CDCl_3$), 29.56 (t, C-10), 45.46 (t, C-12), 46.16 (t, C_α-morpholino), 66.64 (t, C_β-morpholino), 109.87 (d, C-3), 122.29 (s, C-7), 122.61 (d, C-6), 123.30 (d, C-9), 123.60 (d, C-5), 129.00 (d, C-4), 136.64 (s, C-2), 136.74 (d, C-8) and 159.84 (s, C-11). Other examples made by an analogous procedure are listed in Table 1.

1,3-*Dipolar Additions of the Azide* **2**.—(*a*) *With dimethyl acetylenedicarboxylate* (*DMAD*). To a stirred solution of the azide **2** (1 g, 5.5 mmol) in toluene (40 cm^3) at 25 °C DMAD (2.33 g, 16.4 mmol) was added all at once and the mixture was stirred, in the dark, for 3 d at room temperature. After removal of the solvent under reduced pressure the residual oil was chromatographed (Al_2O_3, hexane–ethyl acetate 10:1) to yield dimethyl 1-(1,6-methano[10]annulen-2-yl-1,2,3-triazole-4,5-dicarboxylate **10** ($R^1 = R^2 = CO_2Me$) (0.78 g, 44%), m.p. 112 °C $\delta_H(CDCl_3$, 250 MHz) −0.35 (d, 1 H, *J* 12.5), −0.25 (d, 1 H, *J* 12.5), 3.60 (s, 3 H, Me), 4.00 (s, 3 H, Me), 7.1–7.3 (m, 5 H), 7.52 (d, 1 H) and 7.68 (br, 1 H); *m/z* 325 (M^+) (Found: C, 62.7; H, 4.7; N, 12.8. $C_{17}H_{16}N_3O_4$ requires C, 62.76; H, 4.65; N, 12.92%).

(*b*) *With methyl propiolate*. Under conditions similar to those in (*a*) from the azide **2** (1 g, 5.5 mmol) in toluene (40 cm^3) and methyl propiolate (1.38 g, 16.4 mmol) a mixture of the triazoles **10** ($R^1 = CO_2Me$, $R^2 = H$, $R^1 = H$, $R^2 = CO_2Me$ = 2:1) (0.023 g, 5%) was obtained as an oil; $\delta_H(CDCl_3$, 250 MHz), −0.4 (d, 1 H, *J* 8.3), −0.3 (d, 1 H, *J* 8.3), 3.77 (s, CO_2Me), 3.97 (s, CO_2Me), 6.9–7.4 (m, 7 H), 8.30 (s, 1 H, R^1 in **10**), and 8.47 (s, 1 H, R^2 in **10**) (Found: M^+, 267.1008. $C_{15}H_{13}N_3O_2$ requires *M*, 267.1008 m.s. peakmatching as analysis proved unsatisfactory).

(*c*) *With norbornene*. Conditions similar to those in (*a*) using a solution of the azide **2** (1 g, 5.5 ml) in toluene (40 cm^3) and norborn-2-ene (1.54 g, 16.4 mmol) gave the aziridine **12** (0.22 g, 42%), m.p. 77 °C; $\delta_H(CDCl_3$, 250 MHz), −0.58 (dd, 1 H, *J* 12.5), −0.12 (d, 1 H, *J* 12.5), 0.83 (d, 1 H, *J* 10.4), 1.30 (m, 2 H), 1.54 (m, 3 H), 2.53 (s, 1 H), 2.59 (d, 1 H, *J* 6.3), 2.70 (s, 1 H), 2.91 (d, 1 H, *J* 6.3), 6.50 (d, 1 H, *J* 10.4), 6.85 (t, 1 H, *J* 10.4), 7.05–7.20 (m, 3 H), 7.30 (d, 1 H, *J* 8.3) and 7.65 (d, 1 H, *J* 8.3); *m/z* 249 (Found: M^+, 249.1515. $C_{18}H_{19}N$ requires *M*, 249.1516. Peakmatching because of instability of the product).

Ethyl α-*Azido*-β-*annulenylacrylic Esters* **13**.—To a freshly prepared solution of sodium ethoxide (2.3 g 10 mmol) in dry ethanol (150 cm^3), was added a solution of annulene-2-carbaldehyde (4 g, 23.5 mmol) and ethyl azidoacetate (12.1 g, 93.8 mmol) in dry ethanol (80 cm^3) in the dark at 0 °C. The reaction mixture was agitated for 90 min with the internal temperature ≤20 °C. After removal of the solvent under reduced pressure the residue was neutralised (dil. HCl) and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated under reduced pressure. Final purification was first by chromatography (Al_2O_3, hexane) and then recrystallisation (diethyl ether) to give ethyl α-azido-β-(1,6- methano[10]annulen-2-yl)acrylate **13** ($R^1 = R^2 = H$) (4.5 g, 68%), m.p. 65–67 °C; ν_{max}(KBr)/cm^{-1} 2110 (N_3); $\delta_H(CDCl_3$, 250 MHz), −0.48 (d, 1 H, *J* 10.4), −0.28 (d, 1 H, *J* 10.4), 1.48 (t, 3 H, *J* 8.3, *Me*), 4.37 (q, 2 H, *J* 8.3, CH_2), 7.05 (d, 1 H, *J* 10.4), 7.10–7.60 (m, 6 H) and 7.95 (d, 1 H, *J* 10.4); *m/z* 281 (M^+) (Found: C, 68.55; H, 5.35; N, 14.5. $C_{16}H_{15}N_3O_2$ requires C, 68.31; H, 5.37; N, 14.94%).

Under similar conditions a reaction mixture of sodium ethoxide (2.3 g sodium 10 mmol, in 100 cm^3 ethanol), 1,6-methano[10]annulene-2,7-dicarbaldehyde[18] (2 g, 1.01 mmol) and ethyl azidoacetate (13.33 g, 10.0 mmol) gave after chromatography (Al_2O_3, light petroleum b.p. 60–80 °C: benzene 2:1) and recrystallisation (light petroleum b.p. 60–80 °C methanol) the *diethyl* β,β′-(1,6-*methano*[10]*annulene*-2,7-*diyl*)*bis*-α-*azidoacrylate* **13** [$R^1 = H$, $R^2 = CH{=}C(CO_2Et)N_3$] (2.46 g, 58%), m.p. 104 °C. ν_{max}(KBr)/cm^{-1} 2120 (N_3); $\delta_H(CDCl_3$, 250 MHz), 0.28 (s, 2 H), 1.42 (t, 6 H, *J* 7.5, 2 Me), 4.39 (q, 4 H, *J* 7.5, CH_2), 7.22 (t, 2 H, *J* 9.3), 7.43 (s, 2 H), 7.59 (d, 2 H, *J* 11) and 8.08 (d, 2 H, *J* 11); *m/z* 420 (M^+) (Found: C, 59.9; H, 4.9; N, 19.8. $C_{21}H_{20}N_6O_4$ requires C, 59.99; H, 4.79; N, 19.99%).

[10]*Annulenopyrroles* **14**, **15**.—(*a*) The azidoacrylate **13** ($R^1 = R^2 = H$) (2 g, 7.1 mmol) was dissolved in *p*-xylene (80 cm^3) and the solution kept under reflux for 20 min. After cooling the solvent was driven off under reduced pressure to leave a white solid. Purification by chromatography (Al_2O_3, hexane–ethyl acetate 10:1) or recrystallisation (diethyl ether) yielded *ethyl* 6,11-*methano*[10]*annuleno*[3,2-b]*pyrrole*-2-*carboxylate* **14** (R = H) (1.74 g, 97.4%), m.p. 170 °C; ν_{max}(KBr)/cm^{-1} 3300 and 1675 (CO_2Et); $\delta_H(CDCl_3$, 250 MHz), −0.30 (d, 1 H, *J* 10), 1.05 (d, 1 H, *J* 10), 1.45 (t, 3 H, *J* 7, Me), 3.95 (q, 2 H, *J* 7, CH_2), 6.85–7.48 (m, 7 H) and 9.85 (s, NH); *m/z* 253 (M^+) (Found: C, 75.8; H, 5.95; N, 5.5. $C_{16}H_{15}NO_2$ requires C, 75.86; H, 5.97; N, 5.53%).

(*b*) In a one-pot reaction 5-*tert*-butoxy[10]annulene-2-carbaldehyde **1** (R^1 = CHO, R^2 = Bu′O) (10 g, 41 mmol), ethyl azidoacetate (21 g, 16 mmol), sodium ethoxide (3.8 g) as an ethanolic solution (150 cm^3) was converted as described in (*a*) above into the crude azido ester **13** (R^1 = Bu′O, R^2 = H). Without purification it was heated in *p*-xylene (150 cm^3) for 20 min to give, after work-up as in (*a*), the *ethyl* 5-*tert*-*butoxylannuleno*[3,2-b]*pyrrole*-2-*carboxylate* **14** (R = Bu′O) (7.3 g, 55%), m.p. 178 °C; ν_{max}(KBr)/cm^{-1} 3300 (NH) and 1660 (CO_2Et); $\delta_H(CDCl_3$, 250 MHz), −0.2 (d, 1 H, *J* 8.4), 1.35 (d, 1 H, *J* 8.4), 1.40 (t, 3 H, *J* 6.3 Me), 1.55 (s, 9 H, Me_3), 4.45 (q, 2 H, *J* 6.3, CH_2), 6.54 (s, 1 H), 7.0–7.4 (m, 5 H) and 10.8 (s, 1 H, NH); *m/z* 325 (M^+) (Found: C, 73.85; H, 7.25; N, 4.25. $C_{20}H_{23}NO_3$ requires C, 73.85; H, 7.08; N, 4.31%).

(*c*) Thermolysis of the ester **13** [$R^2 = CH{=}C(CO_2Et)N_3$, $R^1 = H$] (2.46 g, 5.84 mmol) in *p*-xylene (100 cm^3) under conditions described in (*a*) furnished, after purification of the product as in (*a*), the [10]*annuleno*[3,2-b:8,7-b′]*dipyrrole*-2,8-*dicarboxylate* **15** (1.69 g, 85%), m.p. 197 °C; ν_{max}/cm^{-1} 3297 (NH) and 1658 (CO_2Et); $\delta_H(C_5D_5N$, 250 MHz), 0.56 (s, 2 H), 1.22 (t, 6 H, *J* 7.5 Me), 4.37 (q, 4 H, *J* 7.5, CH_2), 7.29–7.86 (m, 6 H) and 13.30 (s, NH); *m/z* 364 (M^+) (Found: C, 69.6; H, 5.5; N, 8.1. $C_{21}H_{20}N_2O_4$ requires C, 69.21; H, 5.53; N, 7.69%).

[10]*Annulenopyridines* **18**.—The α-azido-β-annulenylacrylic ester **13** ($R^1 = R^2 = H$) (0.75 g, 2.7 mmol) was dissolved in dry diethyl ether (25 cm^3) and triphenylphosphine (0.7 g, 2.7 mmol) was added in one portion to the solution. When gas evolution (N_2) had subsided the solvent was removed under reduced pressure and the solid residue recrystallised (hexane) to give the pure *triphenylphosphinimine* **16** (1.10 g, 79%), m.p. 66 °C; $\delta_H(CDCl_3$, 250 MHz) −0.68 (d, 1 H, *J* 8.3), −0.13 (d, 1 H, *J* 8.3), 0.82 (t, 3 H, *J* 6.3, Me), 3.73 (q, 2 H, *J* 10.4, CH_2), 6.78–7.0 (m, 4 H), 7.05–7.35 (m, 13 H, 2 C_6H_5 and 3 H), 7.55–7.65 (m, 5 H,

C_6H_5) and 8.55 (d, 1 H, CH=C–); *m/z* 515 (M^+) (Found: C, 78.9; H, 6.0; N, 3.05. $C_{34}H_{30}NO_2P$ requires C, 79.19; H, 5.87; N, 2.72%).

(*a*) To a solution of the above iminophosphorane (2.18 g, 4.23 mmol) in dry toluene (20 cm^3) were added phenyl isothiocyanate (0.542 g, 4.23 mmol) and the reaction mixture was agitated for 30 min at 0 °C. This was followed by heating under reflux for 10 h and finally by stirring for 3 d. The yellow precipitate was filtered off and washed on the filter (3 × 20 cm^3 hexane). Recrystallisation (CH_2Cl_2–hexane 1:1) yielded *ethyl* 4-*anilino*[10]*annuleno*[3,2-c]*pyridine*-2-*carboxylate* **18** (R = Ph) (1.16 g, 77%), m.p. 156 °C; ν_{max}/cm^{-1} 3418 (NH); $\delta_H(CDCl_3$, 250 MHz), −0.22 (d, 1 H, *J* 9.5), 0.87 (d, 1 H, *J* 9.5), 1.49 (t, 3 H, *J* 8.44, Me), 4.50 (m, 2 H, CH_2), 7.02 (t, 1 H, *J* 7.5), 7.15 (m, 3 H), 7.28–7.41 (m, 5 H, Ph), 7.49–7.59 (m, 3 H, NH + 2 H) and 8.61 (s, 1 H); *m/z* 356 (M^+) (Found: C 77.30; H, 5.45; N, 7.80. $C_{23}H_{20}N_2O_2$ requires C, 77.50; H, 5.65; 7.86%).

(*b*) A mixture of allyl isothiocyanate (0.27 g, 2.83 mmol), the iminophosphorane **16** (1.27 g, 2.83 mmol), and toluene (15 cm^3) was treated as in (*a*). Purification of the crude product by chromatography (SiO_2, hexane–ethyl acetate 10:1) gave *ethyl* 4-*allylamino*[10]*annuleno*[3,2-c]*pyridine*-2-*carboxylate* **18** (R = $CH_2CH{=}CH_2$) (0.62 g, 69%), m.p. 68 °C; ν_{max}/cm^{-1} 3405 (NH); $\delta_H(CDCl_3$, 250 MHz), −0.36 (d, 1 H, *J* 9.5), 0.72 (d, 1 H, *J* 9.5), 1.45 (t, 3 H, *J* 8.3, Me), 4.33 (m, 2 H), 4.46 (q, 2 H, *J* 8.2, CH_2), 5.13–5.39 (m, 2 H), 6.02–6.19 (m, 1 H), 6.97–7.56 (m, 6 H + NH) and 8.35 (s, 1 H); *m/z* 320 (M^+) (Found: C, 74.85; H, 6.2; N, 8.85. $C_{20}H_{20}N_2O_2$ requires C, 74.98; H, 6.29; N, 8.74%).

(*c*) A mixture of tolyl isocyanate (0.48, 3.59 mmol) iminophosphorane **16** (2.18 g, 3.59 mmol) in toluene (25 cm^3) was stirred for 30 min and then heated under reflux (15 h). Stirring was continued at room temperature (24 h). Addition of hexane (60 cm^3) gave a yellow precipitate which was filtered off, washed (3 × 20 cm^3 hexane) and purified (SiO_2, ethyl acetate–light petroleum b.p. 60–80 °C, 1:1) to give ethyl p-*toluidino*[10]-*annuleno*[3,2-c]*pyridine*-2-*carboxylate* **18** (R = C_6H_4Me-*p*) (0.97 g, 73%), m.p. 147 °C; ν_{max}/cm^{-1} 3415 (NH); $\delta_H(CDCl_3$, 250 MHz) −0.28 (d, 1 H, *J* 9), 0.82 (d, 1 H, *J* 9), 1.48 (t, 3 H, *J* 8.2, Me), 2.30 (s, 3 H, Me), 4.48 (m, 2 H, CH_2), 7.07–7.15 (m, 5 H), 7.15 (m, 3 H), 7.38–7.42 (m, 5 H), 7.50–7.56 (d, 1 H, *J* 4.5, NH) and 8.56 (s, 1 H); *m/z* 370 (M^+) (Found, C, 77.95; H, 6.05; N, 7.65. $C_{24}H_{22}N_2O_2$ requires C, 77.81; H, 5.98; N, 7.56%).

2-*Oxazol*-5-*ylannulenes* **19**.—To a methanolic solution (25 cm^3) of 1,6-methano[10]annulene-2-carbaldehyde (1 g, 5.9 mmol) tosylmethyl isocyanide (1.15 g, 5.9 mmol) in methanol (25 cm^3) was added all at once. This was followed by addition of potassium carbonate (5 g) and more methanol (50 cm^3). After the reaction mixture had been heated under reflux for 1 h, it was cooled, evaporated under reduced pressure and the resulting solid washed (ethyl acetate; 5 × 50 cm^3). Chromatography of the latter (SiO_2, hexane–ethyl acetate = 10:1) gave the pure *title compound* **19** (R = H) (1.1 g, 90%), m.p. 73 °C; $\delta_H(CDCl_3$, 250 MHz) −0.40 (d, *J* 9.3), −1.8 (d, *J* 9.3), 7.05–7.25 (m, 3 H), 7.37–7.50 (m, 4-H), 7.79 (d, 1 H) and 7.95 (s, 1 H); *m/z* 209 (M^+) (Found: C, 80.1; H, 5.4; N, 6.65. $C_{14}H_{11}NO$ requires C, 80.35; H, 5.30; N, 6.70%). The methoxy aldehyde **1** (R^1 = CHO, R^2 = OMe) (1 g, 5 mmol) tosylmethyl isocyanide (1.0 g, 5.1 mmol) gave, under the same conditions, 2-*methoxy*-5-*oxazol*-5-*yl*[10]*annulene* **19**; (R = OMe) (1.10 g, 92%), m.p. 114 °C; $\delta_H(CDCl_3$, 250 MHz) −0.58 (d, 1 H, *J* 9.9), 0.44 (d, 1 H, *J* 9.9), 3.86 (s, 3 H, OMe), 6.35 (d, 1 H, *J* 10.2), 7.2–7.3 (m, 3 H), 7.38 (s, 1 H), 7.62 (m, 2 H) and 7.95 (s, 1 H) (Found: C, 74.1; H, 5.35; N, 5.85. $C_{15}H_{13}NO_2$ requires C, 73.99; H, 5.77; N, 6.16%). The butoxy aldehyde **1** (R^1 = CHO, R^2 = Bu^{t}O) (1 g, 4.1 mmol) and tosylmethyl isocyanide (0.81 g, 4.1 mmol) gave, under similar conditions, 2-tert-*butoxy*-5-*oxazol*-5-*yl*-[10]*annulene* (1.1 g, 95%) as an oil. $\delta_H(CDCl_3$, 250 MHz) −0.59 (d, *J* 10), 0.8 (d, 1 H, *J* 10), 1.40 (s, 9 H, 3Me), 6.68 (d, 1 H, *J* 10), 7.15–7.20 (m, 2 H), 7.25 (d, 1 H, *J* 10), 7.38 (s, 1 H), 7.6–7.7 (m, 2 H) and 7.95 (s, 1 H); *m/z* 281 (M^+) (Found: C, 77.0; H, 6.8; N, 4.95. $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%).

Acknowledgements

Support by the Verband der Chemischen Industrie-Fonds der Chemie is gratefully acknowledged. We also thank BASF AG, Bayer AG and Hoechst AG for the donation of chemicals, and are indebted to Mrs. G. Baumann, Miss A. Schormann, Apotheker Th. Eichinger and Z. Sui for recording NMR spectra, to Mr. H. Rudy for measuring mass spectra, and to Mr. P. Weyrich and Mr. G. Beutel for performing microanalyses and measuring IR and UV spectra. This paper is dedicated to Professor S. Hünig (Würzburg) on the occasion of his 70th birthday.

References

1 (*a*) B. Iddon, O. Meth-Cohn, E. F. V. Scriven, H. Suschitzky and P. T. Gallagher, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 900; (*b*) P. A. S. Smith in *Azides and Nitrenes*, ed. E. F. V. Scriven, Academic Press, London, 1984, p. 95; (*c*) F. Hollywood, E. F. V. Scriven, H. Suschitzky, D. R. Thomas and S. E. Carrol, *J. Chem. Soc., Chem. Commun.*, 1978, 806.
2 T. Sheradsky in *Chemistry of the Azido-group*, ed. S. Patai, Interscience Publishers, London, N.Y., Sydney, Toronto, 1971, p. 373.
3 H. Suschitzky, W. Kramer, R. Neidlein and H. Uhl, *J. Chem. Soc., Perkin Trans. 1*, 1988, 983; C. M. Daly, B. Iddon, H. Suschitzky, U. Jordan and F. Sauter, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1933.
4 E. Vogel, W. Schröck and W. A. Böll, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 732.
5 P. A. S. Smith, C. D. Rowe and L. B. Bruner, *J. Org. Chem.*, 1969, **34**, 3430.
6 E. Vogel and W. A. Böll, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 642 and references cited.
7 W. Lange, W. Haas, H. Schmickler and E. Vogel, *Heterocycles*, 1989(2), **28**, 633.
8 O. L. Chapman and J.-P. LeRoux, *J. Am. Chem. Soc.*, 1978, **100**, 282.
9 Y. Nagawa, K. Honda and H. Nakanishi, *J. Chem. Soc., Chem. Commun.*, 1989, 989.
10 G. L'Abbé, *Chem. Rev.*, 1968, **69**, 345.
11 F. S. A. Anet, *Can. J. Chem.*, 1969, **39**, 789.
12 G. Smolinski and C. A. Pryde, *J. Org. Chem.*, 1968, **33**, 2411; H. Hemetsberger, D. Knittel and H. Weidmann, *Monatsh. Chem.* 1969, **100**, 1599; H. Hemetsberger, J. Spira and W. Schönfeld, *J. Chem. Res.*, 1977, (*S*) 247, (*M*) 2701; H. Hemetsberger and D. Knittel, *Monatsh. Chem.*, 1972, **103**, 194; R. E. Bolton, C. J. Moody, M. Pass, C. W. Rees and G. Tojo, *J. Chem. Soc., Perkin Trans 1*, 1988, 2491.
13 W. M. Jones, R. A. Labar, U. H. Brinker and P. H. Gerbert, *J. Am. Chem. Soc.*, 1977, **92**, 6379.
14 G. Hartz and R. Neidlein, *Helv. Chim. Acta*, 1985, **68**, 255.
15 P. Molina and P. M. Fresneda, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1819; P. Molina and P. M. Fresneda, *Synthesis*, 1989, 878; P. Molina, A. Tarrago and M. J. Lidon, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1727.
16 A. M. Van Leusen, B. E. Hoogenboom and H. Siderius, *Tetrahedron Lett.*, 1972, 2369; A. M. van Leusen, *Lect. Heterocycl. Chem.*, 1980, **5**, 111.
17 E. Vogel and W. A. Böll, *Angew. Chem., Int. Ed. Engl.*, 1964, **18**, 784.
18 R. Neidlein and H. Zeiner, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 204.

Paper 0/04272B
Received 19*th September* 1990
Accepted 14*th November* 1990