New Entry to the Imidazo[4,5-*c*]pyrazole System through Photochemically Induced Sequential Transformations of Substituted Pyrrolo[2,3-*d*]-1,2,3-triazoles: X-Ray Crystal Structure of a Substituted 1,3a,6,6a-Tetrahydroimidazo[4,5-*c*]pyrazole

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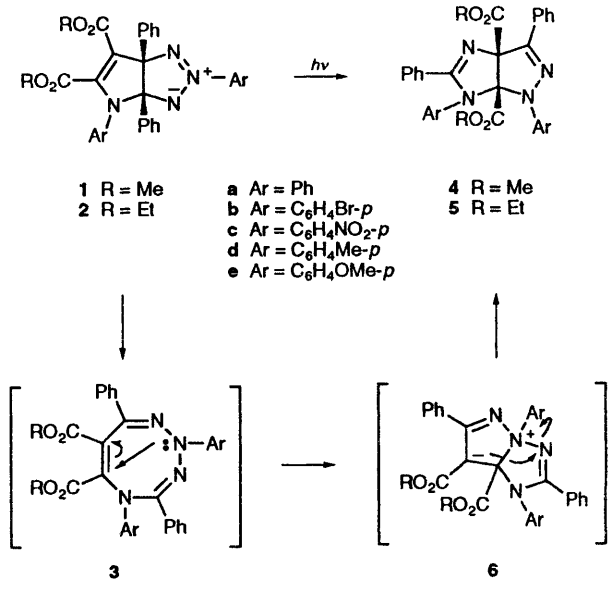
Upon UV irradiation, substituted pyrrolo[2,3-*d*]-1,2,3-triazoles were transformed by a new route to imidazo[4,5-*c*]pyrazoles. The mechanism of the reaction is discussed in terms of a likely 1,2,3,5-tetrazocine intermediate. An X-ray crystal structure of dimethyl 1,6-di(*p*-bromophenyl)-3,5-diphenyl-1,3a,6,6a-tetrahydroimidazo[4,5-*c*]pyrazole-3a,6a-dicarboxylate **4b** is reported.

Despite the growing interest in the imidazo[4,5-*c*]pyrazole system during the past decade because of the pharmacological and photographic applications of its derivatives,[1–3] the ring system is rare[4] and there are few synthetic routes to it.[5] With the exception of cycloaddition of diazomethane to the 4,5-bond of 5-nitroimidazoles[6] the known routes depend on the availability of substituted 5-aminopyrazole derivatives and involve construction of the imidazole ring onto the pyrazole 5-amino substituent.[5,7,8] Herein we report an entirely new high-yield route to the imidazo[4,5-*c*]pyrazole ring system from the easily available ultimate precursor benzil osazone. Recently we have described a high-yield one-pot synthesis of the pyrrolo-[2,3-*d*]-1,2,3-triazoles **1** and **2** from a cycloaddition between the oxidation products of substituted benzil osazones and dialkyl acetylenedicarboxylates.[9] We decided to examine the response of the σ-electrons in the bridgehead bond of **1** and **2** to stimulants in order to explore whether this bond would undergo a disrotatory outward electrocyclic ring expansion to the 10π-tetraazocine structure **3**. This did not occur in thermolytic rearrangement which resulted in cleavage of the pyrrole ring accompanied by ring expansion of the triazole ring. The products were substituted 2,5-dihydro-1,2,3-triazines.[10] Herein we examine the photochemical rearrangement of the series **1** and **2** with UV irradiation. Electrocyclisations may be thermally or photochemically favoured depending on the electron count entering the process. Because of the presence of the lone pairs in the conjugated system the electrocyclic process **1** → **3** can be viewed as either $4n$ or $4n + 2$ but if it is confined to the terminal bond involved it is a $4n$ process requiring irradiation for disrotation. Since it did not occur under thermolytic conditions we expected that it should be favoured under photochemical conditions.



Scheme 1

Results and Discussion

When the series **1** and **2** were irradiated at 350 nm in dry deoxygenated dichloromethane a clean high-yield rearrangement to the imidazo[4,5-*c*]pyrazole compounds **4** and **5** was observed (Scheme 1, Table 1). The structures of the products were indicated by microanalyses and IR spectra as well as highfield ^{1}H and ^{13}C NMR spectra. These spectra showed that a rearrangement had occurred without loss of any fragments and they displayed the signals expected for structures **4** and **5**. An X-ray structure of compound **4b** supported the assignment (Fig. 1) and illustrated interesting conformational constraints in the crowded structure. Thus, in the crystal both of the bridgehead methoxycarbonyl groups were oriented in the same direction with the C=O group pointing towards the imidazole ring and the OMe groups lying out over the pyrazole ring. Dreiding models suggested restricted rotation of the C–C(=O) and C–OMe bonds in these groups because of crowding at the bridgehead. When the OMe groups were replaced by OEt, as in compounds **5**, this restriction showed up in the 270 MHz ^{1}H NMR spectrum when the two EtO groups displayed four overlapping quartets for the two CH_2 moieties each of which behaved as a separate AB system with a small J_{AB} value.

The pathway of this unexpected rearrangement merits careful consideration. The structure of the substrates **1** could allow for an initial transannular 2 + 2 photocycloaddition of the C=C and N=N moieties. However, the resulting prismane-type intermediate would involve fused three- and four-membered rings and would also require the retention of the plus charge on the original azimine nitrogen of **1** and hence it would be highly unlikely. A more likely initial step involves the expected disrotatory opening of the bridgehead C–C bond of **1** to give the 1,2,3,5-tetrazocine system **3**. No tetrazocines containing N–N bonds are known[4] but a 2,3,5,7-tetrazocine has recently been reported.[11] It was originally thought that the 1,2,5,6-tetrazocine **8** was a stable dimerization product of benzil monohydrazone but it was subsequently realised that systems of this potential type preferentially adopt a fused five-membered arrangement.[4,12,13] Thus, the dimerisation product of benzil mono-

Table 1 Substituted imidazo[4,5-*c*]pyrazoles

Compound	M.p. (*T*/°C)	Yield (%)[c]	Mol formula	Found (required) (%) C	H	N
4a	153–154[a]	86	$C_{32}H_{26}N_4O_4$	72.45 (72.45)	5.1 (4.9)	10.2 (10.5)
4b	197–198[a]	80	$C_{32}H_{24}Br_2N_4O_4$	55.9 (55.8)	3.5 (3.5)	8.2 (8.15)
4c	245[b]	82	$C_{32}H_{24}N_6O_8$	61.9 (61.95)	3.85 (3.9)	13.35 (13.55)
4d	190[b]	80	$C_{34}H_{30}N_4O_4$	72.8 (73.1)	5.5 (5.4)	10.05 (10.05)
4e	224[b]	75	$C_{34}H_{30}N_4O_6$	68.9 (69.15)	5.1 (5.1)	9.3 (9.5)
5a	180–181[a]	80	$C_{34}H_{30}N_4O_4$	72.9 (73.1)	5.4 (5.4)	9.7 (10.0)
5b	152–153[a]	83	$C_{34}H_{28}Br_2N_4O_4$	56.9 (57.0)	3.85 (3.9)	7.5 (7.8)
5c	176[b]	70	$C_{34}H_{28}N_6O_8$	62.6 (62.95)	4.2 (4.3)	13.3 (13.0)
5d	145[b]	75	$C_{36}H_{34}N_4O_4$	73.4 (73.7)	6.0 (5.8)	9.3 (9.6)

[a] From hexane. [b] From EtOH. [c] The remainder was recovered substrate **1** or **2**.

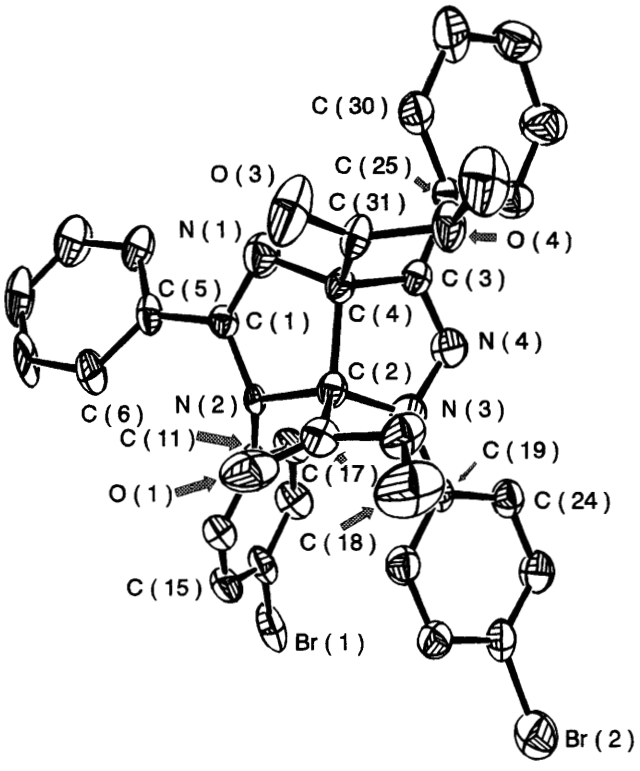
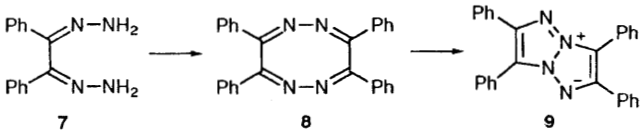


Fig. 1 X-Ray crystal structure of compound **4b**

hydrazone[12] had the bicyclic tetrazapentalene structure **9** and not **8** (Scheme 2). We have repeated and confirmed this by preparing the same compound from benzil dihydrazone **7**. If the condensation product of **7** and benzil had structure **8** it would display only five ^{13}C NMR signals while structure **9** would require ten carbon signals with four from non-protonated carbons. The product **9** presents solubility difficulties for NMR but in the previous work[12] seven definite carbon signals were reported which was enough to rule out structure **8**. Using CD_2Cl_2 as solvent we have observed nine carbon signals for compound **9**. Four of these were singlets in the off-resonance decoupled spectrum. The tenth signal could not be precisely located owing to close overlap of C-3 and C-4 of both phenyl rings. Of course, the formation of **9** from **7** does not require **8** as an intermediate. However, in view of these observations[4,12,13] it is unlikely that the system **3** would be stable. If it were to behave like systems of type **8** then the intermediate **6** would arise. In this, a favourable 1,4-sigmatropic rearrangement involving N–N bond cleavage could replace an N–N bond by an N–C bond and give the products **4**. Such a process would be related to the photoisomerizations involving N–N bond cleavage observed[14] with 3,6-difluoropyridazines.* Hence we view the overall rearrangement process as a photochemically induced series of sequential transformations[15] in the substrates in which the later steps could be thermal or photochemical.



Scheme 2

Experimental

M.p.s were measured on an Electrothermal apparatus. NMR spectra were measured on a JEOL GX FT 270 spectrometer using deuteriochloroform as solvent. *J*-Values are given in Hz. The substrates **1** and **2** were prepared as previously described.[9] The following are typical examples for the preparation of compounds **4** and **5**.

(i) *Preparation of Imidazo*[4,5-c]*pyrazole* **4a**. A solution of compound **1a** (350 mg, 0.66 mmol) in dry dichloromethane (15 cm^3) was flushed with nitrogen and irradiated at 350 nm for 24 h in a quartz cell at ambient temperature. The solvent was removed under reduced pressure and the residue was crystallised from hexane to give white plates of **4a**, *dimethyl* 1,3,5,6-*tetraphenyl*-1,3a,6,6a-*tetrahydroimidazo*[4,5-c]*pyrazole*-3a,6a-*dicarboxylate*, m.p. 153–154 °C (from hexane) (320 mg, 86%); $\delta_H(CDCl_3)$ 3.5 (3 H, s, OMe), 3.7 (3 H, s, OMe), 6.69 (2 H, m), 6.81–7.54 (16 H, m) and 8.20 (2 H, m) all aromatic-H; δ_C 53.1 and 53.2 (MeO), 97.8, 98.0 (C-3a, C-6a), 138.4 (C-3), 143.1 (6-Ph, C-1′), 148.3 (1-Ph, C-1′), 166.0 (C-5), 167.5 (ester C=O), 168.6 (ester C=O), remaining aromatic-C: 116.9, 122.0, 127.6, 128.0, 128.4, 129.05, 129.2, 129.6, 130.5, 130.8 and 131.8 (signal overlap at 128.4 prevented precise location of three aromatic CH signals).

(ii) *Preparation of Imidazo*[4,5-c]*pyrazole* **5c**. Similar treatment of **2c** followed by crystallisation of the residue from ethanol gave yellow flaky crystals of the *imidazo*[4,5-c]*pyrazole* **5c**, m.p. 176 °C (from EtOH) (70%); $\delta_H(CDCl_3)$ 1.03 (3 H, t, Me), 1.16 (3 H, t, Me), 4.05–4.3 (4 H, four overlapping quartets, ester CH_2O), 6.78 (2 H, d) and 7.88 (2 H, d) (6-$C_6H_4NO_2$-*p* AA^1BB^1, J_{AB} 9.5, H_{ortho}, H_{meta} resp.), 8.03 (2 H, d) and 8.21 (2 H, d) (1-$C_6H_4NO_2$-*p* AA^1BB^1, J_{AB} 8.15, H_{meta} and H_{ortho}) and 7.18–7.5 (10 H, m, 3-Ph and 5-Ph); δ_C 13.75 and 13.76 (Me), 62.9 and 63.8 (CH_2O), 96.0, 98.8 (C-3a, C-6a), 132.9 (C-3), 147.6, 124.5 and 141.0 (1-$C_6H_4NO_2$-*p*, C-1′, C-2′, C-4′ resp.), 151.2, 113.7 and 143.6 (6-$C_6H_4NO_2$-*p*, C-1′, 3-2′, C-4′ resp.), 165.2 (C-5), 166.1 and 166.9 (C=O) remaining aromatic: 124.8,

* A referee has pointed this out.

Table 2 Crystal data for **4b**

Crystal size (mm)	0.50 × 0.45 × 0.10
Formula	$C_{32}H_{24}Br_2N_4O_4$
M (amu)	688.374
Monoclinic	
Space group	$P2_1/n$
a/Å	15.384(2)
b/Å	13.476(2)
c/Å	15.562(1)
β/°	113.92(2)
U/Å^3	2949(10)
Z	4
D_c/g cm^{-3}	1.55
μ/cm^{-1}	27.1
F(000)	1384
Radiation Mo-Kα	
Graphite monochromator	λ = 0.710 69 Å
Diffractometer	Enraf–Nonius CAD4F
Orienting reflections, range	25, 13 < θ < 20°
Temperature/°C	22
Scan method	ω–2θ
Data collection range	4 < 2θ < 64°
No. unique data	10 214
Total $I > 2\sigma I$	3524
No. of parameters fitted	380
R,[a] R[b]	8.11%, 8.57%
Quality-of-fit indicator[c]	1.61
Largest shift/esd, final cycle	< 0.001
Largest positive peak (e Å^{-3})	0.56
Largest negative peak (e Å^{-3})	−0.48

[a] $R = [\Sigma\|\|F_o| - |F_o\|\|]/\Sigma|F_o|$. [b] $R_w = [\{\Sigma_w(|F_o| - |F_c|)^2\}/\{\Sigma_w(|F_o|)^2\}]^{\frac{1}{2}}$; $w = 1/[(\sigma F_o)^2 - 0.008\,26\ F_o{}^2]$. [c] Quality-of-fit = $[\Sigma_w(|F_o| - |F_c|)^2/(N_{obs} - N_{parameters})]^{\frac{1}{2}}$.

128.1, 128.4, 128.6, 129.5, 131.3 and 131.7 (signal overlap at 128.6 prevented precise locations of three aromatic C-3′ signals).

Condensation of Benzil Dihydrazone **7** *with Benzil.*—A solution of benzil dihydrazone **7** (11.9 g, 0.05 mol) and benzil (10.5 g, 0.05 mol) in 2-methoxyethanol (100 cm^3) was heated under reflux for 45 h and then cooled to yield 2,3,6,7-tetraphenyl[1,2,3]triazolo[2,1-*a*][1,2,3]triazole **9** (2.89 g, 13%), m.p. 306–307 °C (from benzene) (lit.,[12] 278 °C) (Found: C, 81.8; H, 4.9; N, 13.8. Calc. for $C_{28}H_{20}N_4$: C, 81.5; H, 4.9; N, 13.6%) $\delta_H(CD_2Cl_2)$ 7.34–7.83 (20 H, m, Ph); $\delta_C(CD_2Cl_2)$ 127.49 (s), 128.17 (d), 128.58 (d), 129.04 (s), 129.44 (d), 129.60 (d), 129.71 (d), 132.28 (s) and 145.60 (s).

X-Ray Crystallography.—Crystal data for compound **4b** are given in Table 2. The structure was solved by direct methods (SHELX86)[16] and refined by full-matrix least-squares using (SHELX76).[17] Data were corrected for Lorentz and polarisation effects but not for absorption. Hydrogen atoms were included in calculated positions with fixed thermal parameters. The non-hydrogen atoms were refined anisotropically. The atomic scattering factors for non-hydrogen and hydrogen atoms and the anomalous dispersion correction factors for non-hydrogen atoms were taken from the literature.[18,19,20] All calculations were performed on a VAX 6610 computer. The ORTEP program was used to obtain the drawings.[21] Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.*

Acknowledgements

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* For full details of the CCDC deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1993, issue 1.

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