Heteropentalenes. The Thermal Addition of 1,3-Dimethylpyrazolo-[1,2-*a*]benzotriazole to Dimethyl Acetylenedicarboxylate

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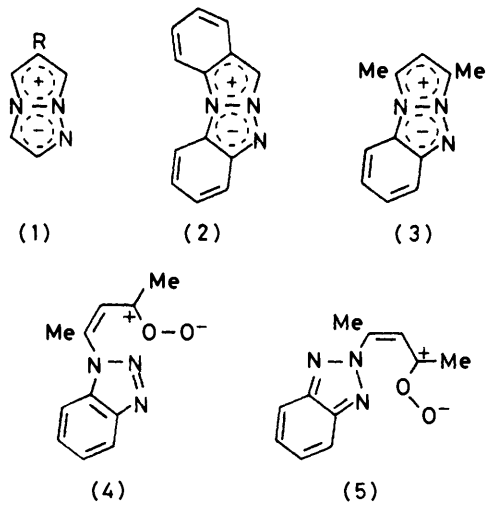
The title compound (3) reacts with dimethyl acetylenedicarboxylate with addition onto the azomethinimine moiety to give dimethyl 2a,4-dimethyl-4a,8b,8c-triazapentaleno[1,6-*ab*]indene-1,2-dicarboxylate (7) *via* a zwitterionic intermediate which can be trapped by protic solvents, *e.g.* methanol or water to give dimethyl 2-[*o*-(3,5-dimethylpyrazol-1-yl)anilino]-3-methoxymaleate (8) or tetramethyl 3,3'-bis-[*o*-(3,5-dimethylpyrazol-1-yl)anilino]-2,2'-oxydimaleate (9), respectively. The cycloadduct (7) undergoes spontaneous retrocycloaddition to dimethyl 3-methylpyrazolo[1,2-*a*]benzotriazole-1,2-dicarboxylate (12) and radical cleavage to yield, unexpectedly, methyl 4,5-dihydro-2-methyl-4-oxopyrazolo-[2,3-*a*]quinoxaline-3-carboxylate (17) as the main product together with small amounts of two benzotriazolylpentenones (14) and (15).

Electrophilic substitution and addition to electron-poor dipolarophiles are the characteristic reactions of the heterocyclic analogues of ' aromatic ' pentalene dianion, or heteropentalenes, as might be expected for compounds with a high lying HOMO. A single formula is no satisfactory representation of these compounds, and different mesomeric zwitterionic formulae must be considered. This led to Ramsden's categorization of these compounds into four classes.[1]

We have recently been concerned with the chemistry of heteropentalenes of Ramsden's Class B, in which two nitrogen atoms occupy the bridging positions, whereas either nitrogen atoms or C–R groups are in the other positions. A typical example is pyrazolo[1,2-*a*]-*v*-triazole, or 1,3a,6a-triazapentalene (1; R = H). From the literature it is known that 5-methyl- and 5-phenyl-pyrazolo[1,2-*a*]triazole (1; R = Me, Ph) undergo cycloaddition with alkynes onto the azomethinylide moiety (*i.e.* across its 3- and 4-position),[2] whereas the dibenzo derivative (2) reacts exclusively at the azomethinimine moiety (N-5).[3] It therefore appeared of interest to explore the regioselectivity of the cycloaddition in the case of a monobenzo derivative, as we have shown that 1,3-dimethylpyrazolo-[1,2-*a*]benzotriazole (3) adds singlet oxygen in both possible directions yielding the zwitterions (4) and (5) which react further to give ketones or epoxy ketones,[4] or are trapped by alcohols to yield hydroperoxides.

At room temperature the heteropentalene (3) reacts completely with an equimolecular amount of dimethyl acetylenedicarboxylate (DMAD) in *ca.* 20 h, and independently from the nature of the solvent. However, different products are obtained under different experimental conditions (Table 1). In aprotic anhydrous solvents (*e.g.* CCl_4, $CHCl_3$, C_6H_6) a single product is formed in *ca.* quantitative yield (n.m.r. spectrum). This product is identified as the [3,5]cycloadduct (7) (Scheme 1) [*e.g.* the vinylic proton with allylic coupling gives an n.m.r. signal (Table 2) at δ 5.0], the aromatic protons producing a singlet at δ 7.0. However, we did not succeed in isolating pure adduct (7) in reasonable yield owing to the number of reactions intervening during the work up (*vide infra*).

On the other hand, a stable product is obtained in the presence of a protic trapping agent. Thus in the presence of methanol (5 : 1 molar ratio) compound (7) never accumulates in detectable amounts (n.m.r. evidence) and the reaction proceeds directly to the stable enamine, (8), which arises from the addition of both DMAD and methanol. The assignment of formula (8) in preference to other possible structures, such as (10), is supported by the easy conversion into 1-(2-aminophenyl)-3,5-dimethylpyrazole (11) by acid-catalysed hydrolysis.



(1) (2) (3) (4) (5)

In the presence of other proton sources, trapping products are likewise formed. Thus, if the starting heteropentalene (3) is used as the crystalline monohydrate, a substantial amount of a compound corresponding to the addition of two molecules of (3), two of DMAD, and one of water is obtained. Mass spectroscopic data and the similarity of n.m.r. and i.r. spectra with those of compound (8) show that this product is the ether (9).

Further observations are pertinent for the reaction in anhydrous media. Thus, if methanol is added after the addition process has been completed, no enamine (8) is formed from adduct (7). Moreover, if the reaction mixture is left at room temperature after the initial addition, a further process, which leads to stable products, takes place. Thus a solid crystallizes out and after 60 h the adduct (7) is practically consumed; work-up of the reaction mixture then affords several products in fair total yield (Scheme 2). These products include two minor products, which were recognized as being identical with the benzotriazolylpentenones (14) and (15) previously obtained by photo-oxidation of compound (3),[4] and two major ones. The molecular formula of the first major product ($C_{14}H_9N_3O_4$) corresponds to the loss of a C_3H_4 unit from the adduct between (3) and DMAD. This product contains one methyl and two methoxy groups and is generally

Table 1. Product yields from the reaction of the heteropentalene (3) with DMAD

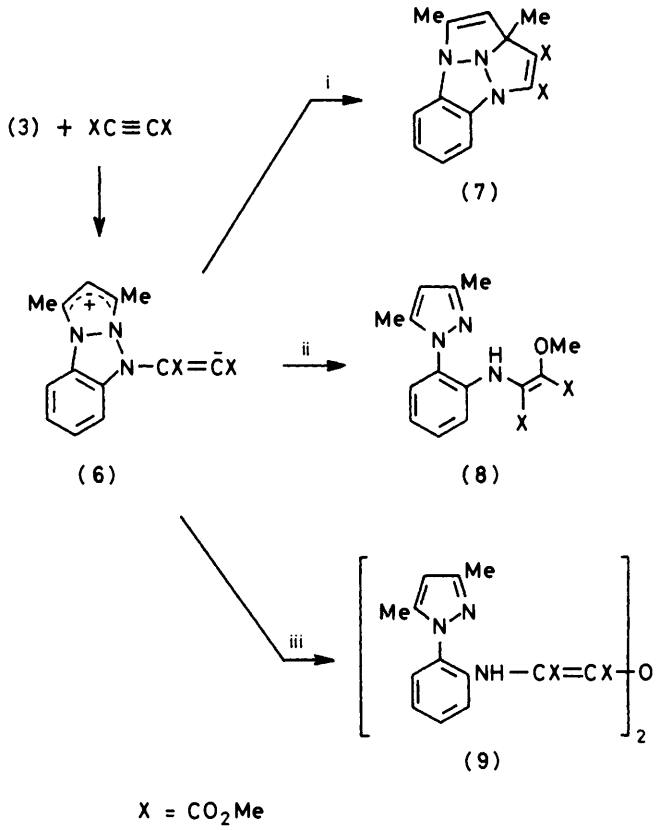
Solvent [a]	Conditions	Reaction time (h)	Yield (%) (7)	(8)	(9)	(12)	(14)	(15)	(17)
CCl_4	Anhydrous	20	100 [b]						
CCl_4	MeOH, 5 equiv.	20		65					
CCl_4	H_2O, 1 equiv.	20			16 [c]				
CCl_4	Anhydrous	70				14	4	4	37

[a] Similar yields in chloroform or benzene under the same conditions. [b] By n.m.r. After chromatographic separation poor yields of compounds (7), (12), (14), (15), and (17) are obtained. [c] Poor yields of compounds (7), (12), (14), (15), and (17) are also obtained.

Table 2. Relevant spectroscopic characteristics for new compounds [a]

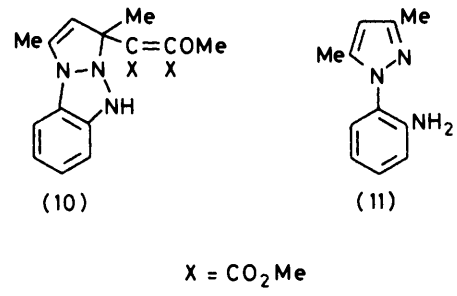
	^{1}H N.m.r. (δ values) Me	MeO	CH	NH	I.r. [b]
(7) [c]	1.6, 1.9	3.65, 3.8	5		1 720, 1 620
(8) [d]	2.2, 2.3	3.6, 3.8	6	8	3 300, 1 730, 1 695, 1 610, 1 600
(9) [d]	2.3	3.5, 3.8	6	8.4	3 240, 1 740, 1 700, 1 595
(12) [d]	2.6	3.9			1 730, 1 680
(17) [d,e]	2.6	3.95		10.3	2 900—3 200, 1 735, 1 640, 1 620
(18) [f]	2.4	3.3	6.9	11.7	2 900—3 200, 1 675, 1 635, 1 600
(19) [d]	2.65		7.05—9.4		1 595, 1 560, 1 520

[a] The molecular peak was in every case prominent in the mass spectrum. [b] In Nujol mull or in KBr. [c] N.m.r. in CCl_4. [d] N.m.r. in $CDCl_3$. [e] ^{13}C N.m.r. in $CDCl_3$: δ_C 13.8 (q), 52.0 (q), 116.2 (d), 116.6 (d), 124.3 (d), 127.5 (d). [f] N.m.r. in $(CD_3)_2SO$.



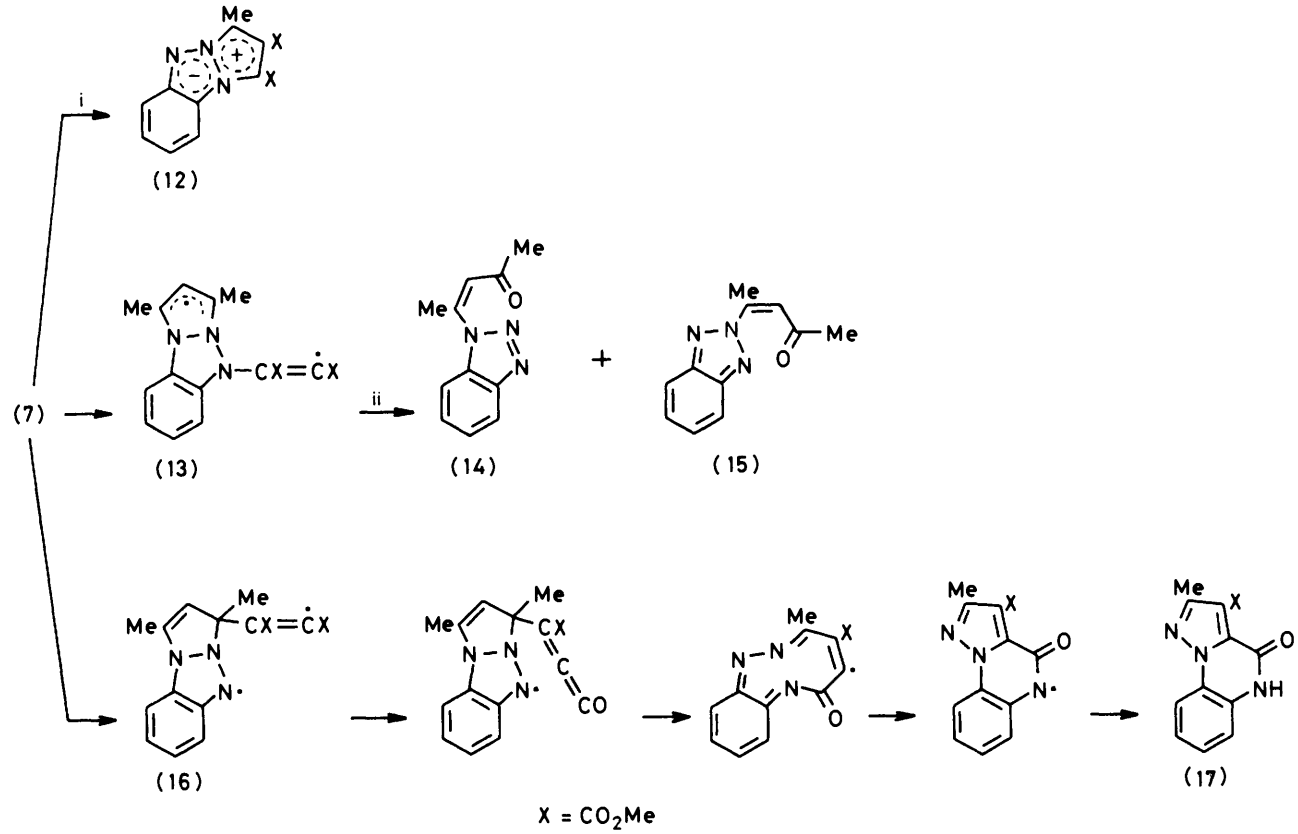
Scheme 1. *Conditions:* i, aprotic medium; ii, MeOH; iii, water

similar in its spectroscopic properties to the starting heteropentalene (3). Thus the structure of dimethyl 3-methylpyrazolo[1,2-*a*]benzotriazole-1,2-dicarboxylate (12) is assigned to this product. As for the second and main product (17), a colourless, blue-fluorescing solid, which in part crystallizes

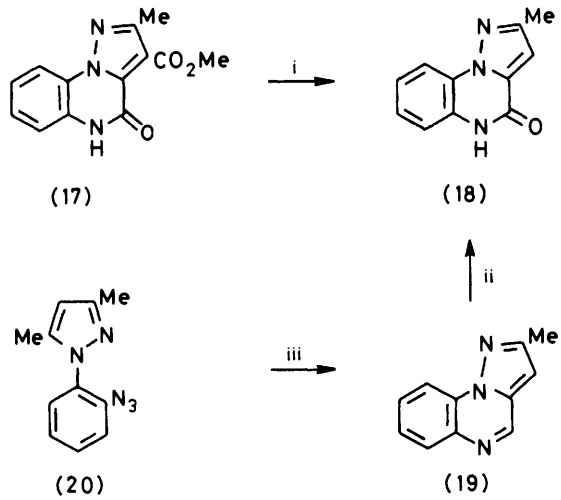


out of the reaction mixture, elemental analysis and mass spectra show that a C_4H_7O unit has been lost from the formula of the monoadduct. ^{13}C and ^{1}H N.m.r. spectra show that one methyl, one methoxy and four C–H groups are present, while the i.r. spectrum shows a strongly chelated N–H group as well as amide and ester groups. This product is resistant to catalytic hydrogenation and is easily hydrolysed under acidic or basic conditions to the corresponding carboxylic acid. On heating at 190 °C with hydrochloric acid the carboxylic group is lost yielding product (18), which retains the main spectroscopic characteristic of the starting ester and shows a singlet at δ 6.9 for an additional C–H group. On the basis of this evidence the structure methyl 4,5-dihydro-2-methyl-4-oxopyrazolo[2,3-*a*]quinoxaline-3-carboxylate (17) is proposed for this product. Final proof was obtained by independent synthesis. Thus the decarboxylated derivative (18) was prepared by oxidation of the pyrazoloquinoxaline (19) with peracetic acid. Compound (19) is a product from the triplet-sensitized decomposition of azide (20) (Scheme 3).[5]

As for the mechanism of the addition between the heteropentalene (3) and DMAD, the u.v. and n.m.r. spectra show no evidence of the preliminary formation of a charge-transfer complex, or indeed of any intermediate, the spectrum of the starting material gradually and continuously evolving into that of the end-product (7). Moreover, in the presence of methanol, no (7) is formed in detectable amounts during the reaction. That the enamine (8) does not arise by alcoholysis



Scheme 2. i, – MeC≡CH; ii, + O_2



Scheme 3. *Reagents and conditions:* i, HCl, 190 °C; ii, AcOH, H_2O_2, 60 °C; then Ac_2O, room temperature; iii, Me_2CO, *hν*

of the adduct (7) is further shown by the fact that methanol does not affect the decomposition of preformed (7) (*vide supra*).

Thus we conclude that the addition of DMAD to the heteropentalene (3) is a two-step process, including a slow reaction to the zwitterion (6), which then undergoes fast closure to the cycloadduct (7) or reaction with protic solvents to afford products such as (8) and (9). There is no equilibrium back to the zwitterion once the tetracyclic adduct (7) is formed (see Scheme 1). However, the cycloadduct is unstable, probably due to steric constraints, and undergoes spontaneous decomposition along different pathways. These include retrocycloaddition liberating propyne and yielding the new stabilized heteropentalene (12), and different types of radical cleavage. In fact, the formation of ketones (14) and (15) can best be understood as occurring by oxygen trapping of the diradical intermediate (13) (see Scheme 2).

As for the main product (17), it does not arise from compound (12). Therefore, the loss of a methoxy group precedes the retrocycloaddition with elimination of propyne. Thus, product (17) can be rationalized from the concurrent diradical intermediate (16), from which loss of a methoxyl radical would be logically followed by formation of a new N–C bond (see Scheme 2). After detachment of propyne, formation of the stable quinoxalone ring affords the driving force for the further rearrangement to the end-product. Support for the radical nature of this decomposition process is found in the fact that gaseous hydrochloric acid does not favour the formation of product (17).

Thus addition of DMAD to the heterocyclic betaine (3) occurs regiospecifically and *via* a zwitterionic intermediate which can be trapped, rather than in a concerted fashion. Results from the addition reaction of other heterocyclic betaines, *e.g.* the formation of vinylic adducts (Michael addition) rather than cycloadducts, or of 2 : 1 adducts,[3c,d,6] suggest that, in other cases also, a stepwise ionic mechanism is followed. On the other hand the cycloadduct (7) decomposes *via* a radical rather than ionic mechanism, with preferential fission of the C-1–N bond.

Experimental

N.m.r. spectra (^1H and ^{13}C) were recorded on a Perkin-Elmer R-12 instrument or a Brucker WP80 instrument, using Me_4S

Table 3. Analytic characteristics of new compounds

Compd.	M.p. (°C)	Crystallization solvent	Formula	Elemental analysis (%) Found C	Found H	Found N	Required C	Required H	Required N
(8)	104—105	Cyclohexane	$C_{18}H_{21}N_3O_5$	60.4	5.9	11.8	60.2	5.9	11.7
(9) [a]	121—122	Benzene	$C_{34}H_{36}N_6O_9 \cdot C_6H_6$	64.3	5.7	11.1	64.0	5.6	11.2
(12)	104—106	Cyclohexane	$C_{14}H_{13}N_3O_4$	58.2	4.5	14.3	58.5	4.6	14.6
(17)	233—235	Benzene	$C_{13}H_{11}N_3O_3$	60.6	4.2	16.3	60.7	4.3	16.3
(18)	>300	Methanol	$C_{11}H_9N_3O$	66.0	4.5	20.8	66.3	4.5	21.1
(19)	85.5—86	Light petroleum b.p. 40—60 °C	$C_{11}H_9N_3$	72.0	4.9	23.0	72.1	4.9	22.9

[a] This product is obtained as yellow prisms containing one molecule of solvent of crystallization.

as internal standard; the i.r. spectra were recorded on a Perkin-Elmer 257 spectrophotometer, and mass spectra on a Dupont 492/B machine. M.p.s are uncorrected. Analytical data are given in Table 3.

1,3-Dimethylpyrazolo[1,2-*a*]benzotriazole (3) was prepared and purified as described elsewhere.[5] Commercial (Merck and Carlo Erba) spectroscopic grade solvents were used after distillation (after treatment with Na_2CO_3 in the case of chlorinated solvents). Dimethyl acetylenedicarboxylate (DMAD) (Fluka) was freshly distilled before use. Column chromatography was performed with silica gel 60 HR (Merck).

General Procedure for the Addition.—1,3-Dimethylpyrazolo-[1,2-*a*]benzotriazole hydrate (1.03 g, 5 mmol) was dissolved in CCl_4 (60 ml) (or $CHCl_3$ or benzene) and half of the solvent was distilled off (except for experiments performed under non-anhydrous conditions). To the cooled solution was added DMAD (0.72 g, 5.5 mmol) and the reaction was followed by t.l.c. and n.m.r. spectroscopy. The results are shown in Table 1. In the 70-h experiments a crystalline solid [compound (17)] began to separate after 1 d. In every case the solvent was evaporated off and the residue chromatographed on a silica-gel column with benzene–ethyl acetate mixtures as eluant.

Hydrolysis of Compound (8).—To a solution of compound (8) (72 mg, 0.2 mmol) in acetone (1 ml) was added 1 : 1 hydrochloric acid (0.2 ml) and the mixture was refluxed for 15 min. After being cooled the solution was neutralized with solid $NaHCO_3$ (105 mg). Extraction with diethyl ether and work-up gave 1-(2-aminophenyl)-3,5-dimethylpyrazole (11) (33 mg, 90%) identical (mixed m.p., spectroscopic properties) with an authentic sample.[5]

Attempted Hydrogenation of Compound (17).—Treatment of product (17) with hydrogen in ethanol, acetic acid, or ethanol–HCl, in the presence of a catalyst (PtO_2 or 10% Pd–C) gave no reaction at normal pressure after several hours.

Decarboxylation of Compound (17).—A solution of product (17) (100 mg) in 35% hydrochloric acid (2 ml) was heated in a sealed tube at 190 °C. The initially formed precipitate of the carboxylic acid slowly dissolved. After 17 h the solvent was evaporated off to give compound (18) (70 mg, 90%) as a crystalline material which was recrystallized from methanol (m.p. >300 °C).

Independent Synthesis of Compound (18).—A solution of 1-(2-azidophenyl)-3,5-dimethylpyrazole (20) (250 mg) in acetone (280 ml) was purged with argon and irradiated in an immersion-well apparatus by means of a Philips 125-W high-pressure mercury lamp through a Pyrex filter for 90 min (*ca.* 80% conversion). The solution was evaporated to dryness. The residues from nine such irradiations were combined and chromatographed on silica gel to give 2-methylpyrazolo-[2,3-*a*]quinoxaline (19) (135 mg, 12%) besides other products (see ref. 5).

A mixture of product (19) (100 mg), 35% hydrogen peroxide (1 ml), and acetic acid (2 ml) was heated at 60 °C for 15 h. The solvent was evaporated off and the tarry residue was treated with a few drops of acetic anhydride. Recrystallization from methanol afforded needles (54 mg, 50%), identical with compound (18) (m.p. >300 °C); identical spectroscopic properties.

Acknowledgements

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References

1 C. Ramsden, *Tetrahedron*, 1977, **33**, 3203.
2 H. Koga, M. Hirobe, and T. Okamoto, *Tetrahedron Lett.*, 1978, 1291.
3 O. Tsuge and H. Samura, (*a*) *J. Heterocycl. Chem.*, 1971, **8**, 707; (*b*) *Org. Prep. Proced. Int.*, 1972, **4**, 273; (*c*) *Tetrahedron Lett.*, 1973, 597; (*d*) *Heterocycles*, 1974, **2**, 27.
4 A. Albini, G. F. Bettinetti, and G. Minoli, *J. Chem. Soc., Perkin Trans. 1*, 1983, 581.
5 A. Albini, G. F. Bettinetti, and G. Minoli, *Chem. Lett.*, 1981, 331.
6 K. T. Potts and J. L. Marshall, *J. Org. Chem.*, 1976, **41**, 129.

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