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Reactions of Nitrile Oxides and Nitrilimines with Imidate Esters, the Nitrogen Atom of which forms Part of a Heterocyclic Ring

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Abstract: The cycloaddition reactions of three cyclic imidate esters, 2-ethoxypyrrolin-5-one (**6**), 2-ethoxyisoindol-3-one (**7**) and 2-ethoxy-1*H*-indol-3-one (**8**) with various 1,3-dipoles were investigated. Dipolarophile **6** added only to nitrile oxides; **8** added to nitrile oxides and to nitrilimines; **7** failed to undergo cycloaddition reactions with either nitrile oxides or nitrilimines.

The 1,3-dipolar cycloaddition reaction has been used widely to prepare 5-membered heterocycles.[1] Among the many functional groups which have been used as dipolarophiles are open-chain imidate esters;[2-4] the resulting adducts then lose an alcohol to give the fully aromatic heterocycles. For example, Rajagopalan prepared 1,2,4-oxadiazoles by the reaction of imidate esters with nitrile oxides.[3]

We have recently extended this work to the study of 2-ethoxy-1-azetines (**1**), which may be regarded as imidate esters of the type -C(OEt)=N-, in which the C=N moiety forms part of a 4-membered ring.[5,6] We have also studied[7] the reactions of 4,5-dihydrooxazoles and 4,5-dihydrothiazoles (*e.g.* **2**) (which may be regarded as cyclic imidate esters in which the -OR group forms part of the ring) with various nitrile oxides, to give either cycloadducts (*e.g.* **3**) or the products **4** of rearrangement processes. [We (P. D. K. and R. W.) have also attempted to extend our earlier studies[5,6] on the azetines **1** to the larger ring cyclic imidate esters **5**.[5b]] Such esters are readily accessible by *O*-ethylation of the corresponding amides with Meerwein's reagent (triethyloxonium tetrafluoroborate). However, in our hands they failed to react with nitrile oxides or nitrilimines (see also, Ref. 5b). We conclude that the lack of reactivity is probably a consequence of the reduction in strain in passing from a 4-membered ring to a ring of larger size.

When attempting to increase the reactivity of the C=N double bond in structures **5** towards 1,3-dipoles, we noted that Houk and his co-workers[8] had studied the effect of electron withdrawing, electron releasing and conjugating groups on the energy levels of the reacting partners in 1,3-dipolar cycloaddition reactions. Introduction of a carbonyl (electron withdrawing) group into the ring of the dipolarophile adjacent to the imine double bond should decrease the energy of the HOMO (occupied molecular orbital of highest energy) and the LUMO (unoccupied molecular orbital lowest energy) of the dipolarophile. Assuming that the reactions of

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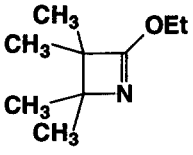
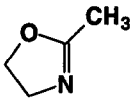
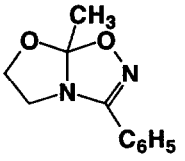
interest here are dipole (HOMO) controlled, as is the norm in *e.g.* nitrile oxide cycloaddition reactions, then such energy changes should facilitate cycloaddition. However, the position of the carbonyl group with respect to the C=N bond and its effect on the reactivity of such dipolarophiles is unclear. An investigation of such chemistry was obviously required. Each of the compounds **6-8** contains a carbonyl group adjacent to the C=N double bond: in **6** and **7** it is at the *N*-terminus of the double bond, whereas in **8** it is at the *C*-terminus.



1



2



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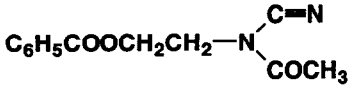
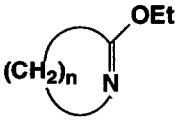


4

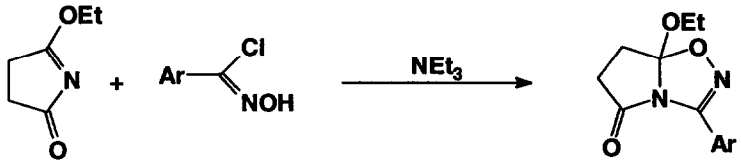


5a; n = 3
5b; n = 4
5c; n = 5

Accordingly, 2-ethoxypyrrolin-5-one **6**,[9] 2-ethoxyisoindol-3-one **7**,[10] and 2-ethoxy-1*H*-indol-3-one **8**[11] were prepared by ethylation of the silver salt of the appropriate amide or imide with ethyl iodide. Surprisingly, *O*-alkylation with Meerwein's reagent was unsatisfactory.

The imidate esters **6** and **8** each formed cycloadducts when treated with a range of nitrile oxides **9a-d** (Sch. 1 and 2). The adducts **10** and **11** showed spectral characteristics (see Experimental section) in accord with the proposed structures, but it was not possible to define with certainty the regiochemistry of the cycloaddition reaction. However, there is ample precedent to suggest that it is as depicted in structures **10** and **11**; in particular, X-ray crystallographic data are available for related structures.[5a,5b]

When the nitrile oxides were generated *in situ* by treatment of the chloro oximes **9** with triethylamine in benzene at 0 °C, the cycloadducts **10** were isolated in yields of 6-28%. In each case, the remaining product from the reaction was essentially the dimer of the nitrile oxide. Yields of cycloadducts were improved (11-49%) if the chloro oximes **9** were thermolysed in toluene at 110 °C.



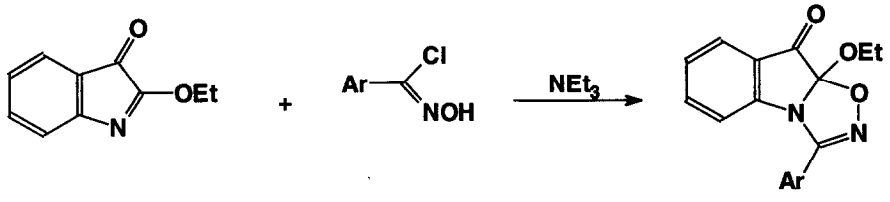
6 9 10

a; Ar = C_6H_5
b; Ar = 4-CH_3O-C_6H_4
c; Ar = 4-NO_2-C_6H_4
d; Ar = C_6H_5CO

Sch. 1. Reaction of Nitrile Oxides with 2-Ethoxypyrrolin-5-one.

When nitrile oxides (generated from their precursor **9** with triethylamine) were allowed to react with the imidate ester **8** (Sch. 2), improved yields of cycloadducts **11** (58-70%) were obtained. We are aware[12a] that other workers have made a brief investigation into the reaction of the methoxy analogue with aromatic nitrile oxides.[12b] It is interesting to note that the nitrile oxide derived from the precursor **9d** gave the expected cycloadducts (**10d** and **11d**), both with **6** and **8**. We have shown earlier[7] that its cycloadducts with 4,5-dihydrooxazoles and related compounds undergo spontaneous rearrangement reactions.

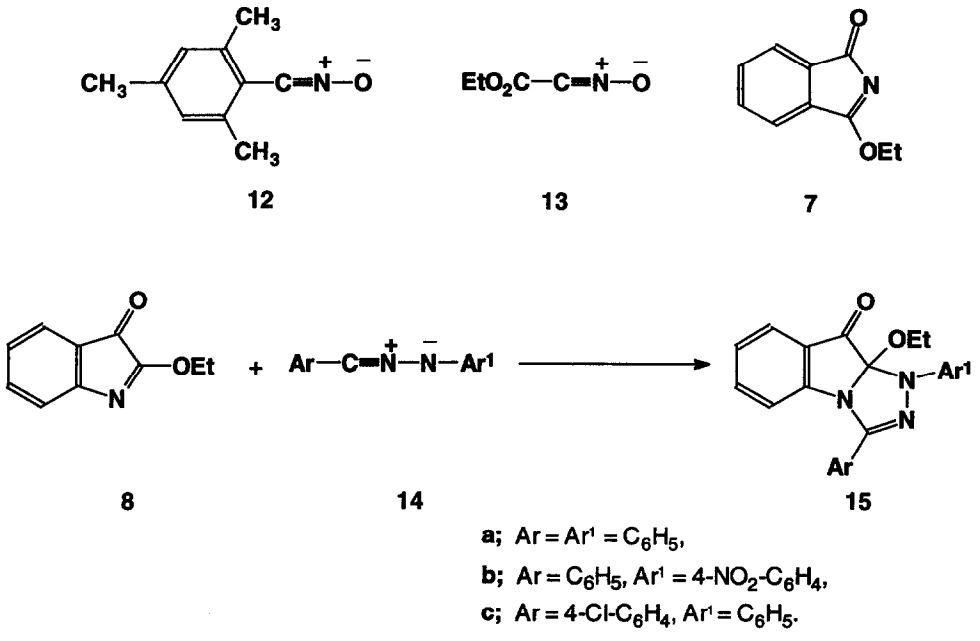
The nitrile oxides **12** and **13** failed to react with any of the dipolarophiles described here, the former presumably because of steric hindrance, the latter because of a reduction in reactivity due to electron delocalisation.



8 9 11

a; Ar = C_6H_5
b; Ar = 4-CH_3O-C_6H_4
c; Ar = 4-NO_2-C_6H_4
d; Ar = C_6H_5CO

Sch. 2. Reaction of Nitrile Oxides with 2-Ethoxy-1*H*-indol-2-one.



Sch. 3. Reaction of Nitrilimines with 2-Ethoxy-1*H*-indol-3-one.

The nitrilimines **14** were prepared *in situ* by dehydrohalogenation of the corresponding hydrazonoyl halides with triethylamine.[13] They gave moderate yields (30-50%) of the adducts **15** (Sch. 3) with **8**, but gave no isolable products with either **6** or **7**. For a reason unknown to us, 2-ethoxyisoindol-3-one **7** failed also to react with any of the nitrile oxides used in the present work.

In summary, we have demonstrated that the C=N double bond in cyclic imidate esters of ring size greater than four will react with selected 1,3-dipoles, provided that the activity of the bond is increased by conjugation with an appropriate carbonyl group.

EXPERIMENTAL

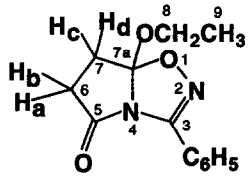
General Experimental Details.

^{1}H and ^{13}C NMR spectra were determined in deuterochloroform solution at 270 and 68 MHz respectively on a JOEL JNM-GX-FT-NMR spectrometer. Chemical shifts are recorded in parts per million (ppm) downfield from tetramethylsilane. IR spectra were determined for KCl discs or liquid films on a Perkin-Elmer PE 783 spectrometer. Mass spectra were determined on a Finnigan-MAT 1020 automated GC/MS instrument. Ether

refers to diethyl ether and light petroleum refers to the fraction of b.p. 40-60 °C. Toluene, benzene and ether were dried over sodium wire, then redistilled.

The α-chloro-oximes **9a-c** were prepared by chlorination of the appropriate aldoxime with t-butyl hypochlorite in propan-2-ol.[14] This reagent was found to be much superior to the commonly used *N*-chlorosuccinimide.[15] The α-chloro-oxime **9d** was prepared by nitrosation of phenacyl chloride.[16]

7a-Ethoxy-3-phenyl-5,6,7,7a-tetrahydropyrrolo[1,2-d][1,2,4]oxadiazol-5-one **10a**.



10a

Triethylamine (4.04 g, 40 mmol) in dry benzene (100 cm^3) was added dropwise during 2 h to a solution of 2-ethoxypyrrolin-5-one (1.27 g, 10 mmol) and benzenecarboximidoyl chloride (1.56 g, 10 mmol) in dry benzene (25 cm^3) at 0 °C. When the reaction was complete (TLC) the precipitated triethylamine hydrochloride was filtered off and the solvent was removed *in vacuo*. The product was purified by column chromatography (silica gel; dichloromethane-hexane, 9:1), then recrystallized from ether-light petroleum, to give colourless needles (0.59 g, 24%), m.p. 131-132 °C (Found: C, 63.2; H, 5.8; N, 11.4. $C_{13}H_{14}N_2O_3$ requires C, 63.4; H, 5.75; N, 11.4%); $\upsilon_{max.}$ 1750 (C=O) 1595, 1550, (C=N), 1055 (C-O-CH_2CH_3), 710 and 695 cm^{-1} (monosubstituted aromatic ring); δ_H 1.35 (3H, q, OCH_2CH_3, $J_{8,9}$ 7.0 Hz), 2.52 (1H, ddd, H_a, J_{ab} 13.0, J_{ac} 9.0, J_{ad} 11.0 Hz), 2.68 (1H, ddd, H_b, J_{ab} 13.0, J_{bc} 1.0, J_{bd} 9.0 Hz), 2.70 (1H, ddd, H_c, J_{ac} 9.0, J_{bc} 1.0, J_{cd} 18.0 Hz), 3.09 (1H, ddd, H_d, J_{ad} 11.0, J_{bd} 9.0, J_{cd} 18.0 Hz), 3.39 (1H, dq, *H-8a*, $J_{8a,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz), 3.58 (1H, dq, *H-8b*, $J_{8b,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz) (The signals H_a, H_b, H_c and H_d relate to the protons CH_aH_b-CH_cH_d, *i.e.* protons attached to C-5 and C-6 in the reduced pyrrole ring; the assignments of the chemical shifts to H_a and H_b may, of course, be reversed, as may those of H_c and H_d), 7.70 (5H, m, Ar*H*); δ_C 14.9 (CH_3), 33.7, 34.7 (C-6 and C-7), 58.6 (OCH_2), 121.6 (C-3), 123.4, 128.5, 128.5, 131.5 (aromatic carbon atoms), 173.7 (C=O); *m/z* 246 (M^+), 217 (M^+-CH_2CH_3) and 119 ($C_6H_5CNO^+$).

7a-Ethoxy-3-(4-methoxyphenyl)-5,6,7,7a-tetrahydropyrrolo[1,2-d][1,2,4]oxadiazol-5-one **10b**.

This was prepared (28%) from **6** and the nitrile oxide precursor **9b** according to the method described for **10a**. The product was purified by column chromatography (silica gel; dichloromethane), then recrystallized from ether-light petroleum. It had m.p. 115-116 °C (Found: C, 61.0; H, 5.8; N, 10.0. $C_{14}H_{16}N_2O_4$ requires C, 60.85; H, 5.85; N, 10.15%); $\upsilon_{max.}$ 1745 (C=O) 1610, 1590 (C=N), 1050 (C-O-CH_2CH_3), 890 and 840 cm^{-1} (1,4-disubstituted aromatic ring); δ_H 1.25 (3H, q, OCH_2CH_3, $J_{8,9}$ 7.0 Hz), 2.51 (1H, ddd, H_a, J_{ab} 13.0, J_{ac} 9.0, J_{ad} 11.5 Hz), 2.68 (1H, ddd, H_b, J_{ab} 13.0, J_{bc} 1.0, J_{bd} 9.0 Hz), 2.70 (1H, ddd, H_c, J_{ac} 9.0, J_{bc} 1.0, J_{cd} 18.0

Hz), 3.08 (1H, ddd, H_d, J_{ad} 11.5, J_{bd} 9.0, J_{cd} 18.0 Hz), 3.39 (1H, dq, *H-8a*, $J_{8a,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz), 3.58 (1H, dq, *H-8b*, $J_{8b,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz), 3.09 (3H, s, OCH_3), 7.71 (5H, m, Ar*H*) (The signals H_a, H_b, H_c and H_d relate to the protons CH_aH_b-CH_cH_d, *i.e.* protons attached to C-5 and C-6 in the reduced pyrrole ring; the assignments of the chemical shifts to H_a and H_b may be reversed, as may those of H_c and H_d); δ_C 15.0 (CH_3), 33.7, 35.0 (C-6 and C-7), 58.8 (OCH_2), 121.5 (C-3), 115.6, 114.1, 130.3, 162.3 (aromatic carbon atoms), 173.9 (C=O); *m/z* 276 (M^+), 231 (M^+ - OCH_2CH_3) and 149 (100%, $CH_3OC_6H_4CNO^+$).

7a-Ethoxy-3-(4-nitrophenyl)-5,6,7,7a-tetrahydropyrrolo[1,2-d][1,2,4]oxadiazol-5-one **10c**.

Prepared (8%) according to the method described for **10a**, this was purified by column chromatography (silica gel; trichloromethane), then recrystallized from ethanol (x 2). It had m.p. 173-174 °C. (Found: C, 53.55; H, 4.55; N, 14.3. $C_{13}H_{13}N_3O_5$ requires C, 53.6; H, 4.5; N, 14.45%); $\upsilon_{max.}$ 1745 (C=O) 1610, 1590, 1520 (C=N), 1525, 1430 (NO_2), 1050 (C-O-CH_2CH_3), 890 and 845 cm^{-1} (1,4-disubstituted aromatic ring); δ_H 1.45 (3H, q, OCH_2CH_3, $J_{8,9}$ 7.0 Hz), 2.50 (1H, ddd, H_a, J_{ab} 13.0, J_{ac} 9.0, J_{ad} 11.5 Hz), 2.68 (1H, ddd, H_b, J_{ab} 13.0, J_{bc} 1.0, J_{bd} 9.0 Hz), 2.71 (1H, ddd, H_c, J_{ac} 9.0, J_{bc} 1.0, J_{cd} 17.0 Hz), 3.09 (1H, ddd, H_d, J_{ad} 11.5, J_{bd} 9.0, J_{cd} 17.0 Hz), 3.38 (1H, dq, *H-8a*, $J_{8a,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz), 3.58 (1H, dq, *H-8b*, $J_{8b,9}$ 7.0, $J_{8a,8b}$ 9.0 Hz), 7.94 (5H, m, Ar*H*) (The signals H_a, H_b, H_c and H_d relate to the protons CH_aH_b-CH_cH_d, *i.e.* protons attached to C-5 and C-6 in the reduced pyrrole ring; the assignments of the chemical shifts to H_a and H_b may be reversed, as may those of H_c and H_d); δ_C 14.9 (CH_3), 34.0, 34.6 (C-6 and C-7), 59.0 (OCH_2), 122.5 (C-3), 123.8, 129.5, 129.7, 149.1 (aromatic carbon atoms), 174.3 (C=O); *m/z* 291 (M^+), 246 (M^+-OCH_2CH_3), 218 (100%, M^+ - OCH_2CH_3 - CH_2=CH_2), 164 ($O_2NC_6H_4CNO^+$).

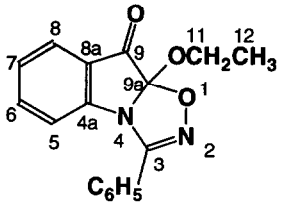
3a-Benzoyl-7a-Ethoxy-5,6,7,7a-tetrahydropyrrolo[1,2-d][1,2,4]oxadiazol-5-one **10d**.

A mixture of *N*-hydroxy-α-oxobenzeneethanimidoyl chloride (0.45 g, 2.5 mmol), 2-ethoxypyrrolin-5-one (0.32 g, 2.5 mmol) and dry toluene (25 cm^3) was heated under reflux for 2h, then the solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel; trichloromethane) and recrystallized from aqueous ethanol, to give white needles (0.34 g, 49%), m.p. 82-83 °C (Found: C, 61.35; H, 5.1; N, 10.5. $C_{14}H_{14}N_2O_4$ requires C, 61.3; H, 5.15; N, 10.2%); $\upsilon_{max.}$ 1760 (ketonic C=O), 1725 (amidic C=O), 1595, 1545 (C=N), 1040 (C-O-CH_2CH_3), 695 and 720 cm^{-1} (monosubstituted aromatic ring); δ_H 1.25 (3H, q*, OCH_2CH_3, $J_{8,9}$ 7.0 Hz), 2.59 (1H, ddd, H_a, J_{ab} 12.0, J_{ac} 4.5, J_{ad} 2.5 Hz), 2.71 (1H, ddd, H_b, J_{ab} 12.0, J_{bc} 0.5, J_{bd} 17.5 Hz), 2.74 (1H, ddd, H_c, J_{ac} 4.5, J_{bc} 7.5, J_{cd} 11.0 Hz), 3.09 (1H, ddd, H_d, J_{ad} 2.5, J_{bd} 17.5, J_{cd} 11.0 Hz), 3.46 (2H, q, *H-8*, $J_{8,9}$ 7.0 Hz), 7.51 (2H, m, Ar*H*), 7.67 (1H, m, Ar*H*) and 8.27 (2H,m, Ar*H*) (The signals H_a, H_b, H_c and H_d relate to the protons CH_aH_b-CH_cH_d, *i.e.* protons attached to C-5 and C-6 in the reduced pyrrole ring; the assignments of the chemical shifts to H_a and H_b may be reversed, as may those of H_c and H_d); δ_C 14.7 (CH_3), 34.4, 35.1 (C-6 and C-7), 59.0 (OCH_2), 121.6 (C-3), 128.7, 128.8, 130.6, 134.9 (aromatic carbon atoms), 173.9 and 179.7 (C=O); *m/z* 274 (M^+), 105 (100%, $C_6H_5CO^+$) and 77 ($C_6H_5^+$).

*The signals corresponding to the two protons H_{8a} and H_{8b} which are adjacent to the chiral centre in this compound are superimposed upon each other.

Preparation of the cycloadducts **10a-c** by the thermolysis of the α-chloro-oxime were carried out according to the procedure described in the preparation of compound **10d**. The products were purified as detailed earlier and the yields were 36%, 39% and 11% for **10a**, **10b** and **10c**, respectively.

9a-Ethoxy-9,9a-dihydro-3-phenyl-1,2,4-oxadiazolo[4,5-a]indol-9-one (**11a**).



11a

The title compound was prepared according to the precedure described earlier for the preparation of **9a**. It was isolated as a gum (62%), after column chromatography (silica gel, trichloromethane) (Found: C, 69.5; H, 4.8; N, 9.45. $C_{17}H_{14}N_2O_3$ requires C, 69.4; H, 4.8; N, 9.5%); $\upsilon_{max.}$1745 (C=O), 1605, 1555, (C=N), 1055 (C-O-CH_2CH_3), 885, 850, 845 (1,2-disubstituted aromatic ring) and 705 and 695 cm^{-1}(monosubstituted aromatic ring); δ_H 1.32 (3H, t, CH_2CH_3, $J_{11,12}$ 7.0 Hz), 3.88 (2H, dq, $CH_{11a}H_{11b}CH_3$, $J_{11a,11b}$ 20, $J_{11,12}$ 7.0 Hz), 6.89 (1H, d, Ar*H*), 7.24 (1H, m, Ar*H*), 7.43 (1H, m, Ar*H*), 7.51 (3H, m, Ar*H*), 7.71 (1H, m, Ar*H*) and 7.90 (2H, m, Ar*H*); δ_C 15.2 (C-12), 60.2 (C-11), 116.4, 125.7, 126.6, 128.9, 132.2, 138.0, 129.3, 132.1 (aromatic carbon atoms), 122.8 (C-3), 125.1, 156.3 (C-5 and 9a), 154.5 (C-10a), 189.5 (C=O); *m/z* 294 (M^+), 249 (M^+ - OCH_2CH_3), 221, (M^+- OCH_2CH_3 - CH_2=CH_2), and 119 (base peak; $C_6H_5CNO^+$).

9a-Ethoxy-3-(4-methoxyphenyl)-9,9a-dihydro-1,2,4-oxadiazolo[4,5-a]indol-9-one (**11b**).

Prepared (70%) according to the procedure described earlier for the synthesis of **10a**, this was isolated from the reaction mixture by column chromatography (silica gel, dichloromethane), then purified by recrystallization from ether-light petroleum. It had m.p. 107-108 °C (Found: C, 66.65; H, 4.95; N, 8.65. $C_{18}H_{16}N_2O_4$ requires C, 66.65; H, 4.95; N, 8.65%); $\upsilon_{max.}$1750 (C=O), 1615, 1520 (C=N), 1050 (C-O-CH_2CH_3), 880, 850 (1,4-disubstituted aromatic ring), and 845 cm^{-1} (1,2-disubstituted aromatic ring); δ_H 1.32 (3H, t, CH_2CH_3, $J_{11,12}$ 7.0 Hz), 3.91 [5H, superimposed q and s, CH_3O and OCH_2CH_3, *J* 7.0 Hz], 6.89 (1H, m, Ar*H*), 7.09 (2H, d, Ar*H*), 7.29 (1H, m, Ar*H*), 7.41 (1H, m, Ar*H*), 7.75 (1H, d, Ar*H*), and 7.86 (2H, d, Ar*H*); δ_C 14.1 (C-12), 60.1 (ArOCH_3), 60.7 (C-11), 114.7, 116.3, 117.0, 125.5, 126.4, 130.5, 137.9, 162.7 (aromatic carbon atoms), 122.7 (C-3), 128.9, 156.0 (C-5 and 9a), 154.5 (C-10a), 189.6 (C=O); *m/z* (No M^+ observed), 279 (M^+ - OCH_2CH_3), 249 (M^+ - OCH_2CH_3 - CO).

9a-Ethoxy-9,9a-dihydro-3-(4-nitrophenyl)-1,2,4-oxadiazolo[4,5-a]indol-9-one (**11c**).

Prepared (58%) according to the method described previously for the synthesis of **10c**, this was isolated from the reaction mixture using column chromatography (silica gel, trichloromethane), then purified by recrystallization from ethanol (x 2) to afford yellow needles, m.p. 173-174 °C (Found: C, 60.1; H, 3.85; N, 12.3. $C_{17}H_{13}N_3O_5$ requires C, 60.2; H, 3.85; N, 12.4%); $\upsilon_{max.}$1745 (C=O), 1620, 1580 (C=N), 1060 (C-O-CH_2CH_3), 885, 850 (1,4-disubstituted aromatic ring), and 845 cm^{-1} (1,2-disubstituted aromatic ring); δ_H 1.36 (3H, t, CH_2CH_3, $J_{11,12}$ 7.0 Hz), 3.85 (2H, dq, $CH_{11a}H_{11b}CH_3$, $J_{11a,11b}$ 20, $J_{11,12}$ 7.0 Hz), 6.88 (1H, m, Ar*H*), 7.33 (1H, m, Ar*H*), 7.49 (1H, m, Ar*H*), 7.81 (1H, m, Ar*H*) 8.13 (2H, m, Ar*H*) and 8.43 (2H, d, Ar*H*); δ_C 15.0 (C-12), 60.3 (C-11), 116.1, 124.5, 126.9, 129.7, 129.7, 138.2, 149.8, 162.6 (aromatic carbon atoms), 122.6 (C-3), 131.4, 154.8 (C-5 and 9a), 153.9 (C-10a), 189.4 (C=O); *m/z* 339 (M^+), 310 (M^+ - OCH_2CH_3).

3a-Benzoyl-9a-ethoxy-9,9a-dihydro-1,2,4-oxadiazolo[4,5-a]indol-9-one (**11d**).

Prepared (56%) by the method described earlier for the synthesis of **10a**, it was obtained as a semi-solid (TLC pure) by means of column chromatography (silica gel, trichloromethane) (Found: C, 67.25; H, 4.45; N, 8.8. $C_{18}H_{14}N_2O_4$ requires C, 67.1; H, 4.4; N, 8.7%); $\upsilon_{max.}$1744, 1715 (ketonic CO), 1605 (C=N), 1055 (C-O-CH_2CH_3), 865, (1,2-disubstituted aromatic ring), and 705 and 695 cm^{-1} (monosubstituted aromatic ring); δ_H 1.32 (3H, t, $CH_{11a}H_{11b}CH_3$, $J_{11,12}$ 7.0 Hz), 3.75 (2H, q, $CH_{11a}H_{11b}CH_3$, $J_{11,12}$ 7.0 Hz), 7.31 (1H, m, Ar*H*), 7.72 (5H, m, Ar*H*), 8.29 (2H, m, Ar*H*); δ_C 14.9 (C-12), 60.3 (C-11), 118.5, 126.4, 128.8, 128.8, 129.7, 130.6, 134.9, 135.0, 138.7 (aromatic carbon atoms), 122.7 (C-3), 126.6, 153.8 (C-5 and 9a), 153.7 (C-10a), 182.1 and 189.4 (2 x C=O); *m/z* (No M^+ observed), 277 (M^+ - OCH_2CH_3) and 249 (M^+ -OCH_2CH_3).

9,9a-Dihydro-1,3-diphenyl-1H-1,2,4-triazolo[4,5-a]indol-9-one (**15a**).

Triethylamine (4.04 g, 40 mmol) and *N*-phenylbenzenecarbohydrazonoyl chloride (2.31 g, 10 mmol) were added successively to a solution of 2-ethoxy-1*H*-indol-3-one **8** (1.75 g, 10 mmol) in dry benzene (50 cm^3). The mixture was stirred at ambient temperature for 3 days then the precipitated triethylamine hydrochloride was filtered off and the solvent was removed *in vacuo*. The crude solid was then purified by column chromatography (silica gel, dichloromethane-light petroleum, 1:1). The virtually pure cycloadduct (1.08 g, 30%), when recrystallized from ethanol had m.p. 123-125 °C (Found: C, 74.8; H, 5.1; N, 11.3 $C_{23}H_{19}N_3O_2$ requires C, 74.8; H, 5.2; N, 11.35%); $\upsilon_{max.}$1730 (CO), 1605, 1600 (CN), 1050 (C-O-CH_2CH_3), 885 (1,4-disubstituted aromatic ring) and 850 cm^{-1} (1,2-disubstituted aromatic ring); δ_H 1.14 (3H, t, CH_2CH_3, $J_{11,12}$ 7.0 Hz), 4.35 (2H, dq, $CH_aH_bCH_3$, $J_{11a,11b}$ 20.0, $J_{11,12}$ 7.0 Hz), 6.85 (3H, m, Ar*H*), 7.12 (3H, m, Ar*H*), 7.40 (4H, m, Ar*H*), 7.98 (2H, m, Ar*H*), and 7.93 (2H, m, Ar*H*); δ_C 14.0 (OCH_2CH_3), 66.3 (OCH_2CH_3), 114.6, 119.9, 121.3, 124.6, 125.1, 125.2, 126.5, 128.7, 129.1, 130.7, 131.5, 132.4, 132.5, 142.7, 152.3, 152.9, and 175.3 (*C*O); *m/z* 369 (M^+), 340 (M^+ - CH_2CH_3), 324 (M^+ - OCH_2CH_3).

9,9a-Dihydro-1-(4-nitrophenyl)-3-phenyl-1H-1,2,4-triazolo[1,2-d]indol-9-one (**15b**).

This was prepared (40%) by a method analogous to that used for **15a**. The product was isolated from the reaction mixture by means of column chromatography (silica gel, hexane-dichloromethane, 1:5) and then recrystallized from ethanol. It had m.p. 189-190 °C (Found: C, 66.55; H, 4.35; N, 13.5. $C_{23}H_{18}N_4O_4$ requires C, 66.7; H, 4.4; N, 13.5%); $\upsilon_{max.}$ 1735 (CO), 1615, 1595 (CN), 1530, 1360 (NO_2), 890, 885, 850, and 840 cm^{-1} (two 1,4-disubstituted aromatic rings); δ_H 1.23 (3H, t, OCH_2CH_3, $J_{11,12}$ 7.0 Hz), 4.48 (2H*, q, CH_2CH_3, $J_{11,12}$ 7.0 Hz), 6.85 (2H, m, Ar*H*), 7.13 (1H, m, Ar*H*), 7.35 (1H, m, Ar*H*), 7.40 (6H, m, Ar*H*), 7.90 (1H, m, Ar*H*), and 8.04 (2H, m, Ar*H*); δ_C 14.1 (OCH_2CH_3), 67.0 (OCH_2CH_3), 112.3, 120.5, 124.2, 124.5, 125.6, 125.8, 125.9, 126.9, 128.9, 129.5, 131.6, 133.6, 140.5, 146.1, 152.1, 154.7 (aromatic carbon atoms, C-9a and C-3), and 173.8 (CO); *m/z* 414 (M^+), 385 (M^+ - CH_2CH_3), 369 (M^+ - OCH_2CH_3).

*The signals corresponding to the two protons which are adjacent to the chiral centre in this compound are superimposed upon each other.

3-(4-Chlorophenyl)-9,9a-dihydro-1-phenyl-1H-1,2,4-triazolo[4,5-a]indol-9-one (**15c**).

This was prepared using a method analogous to that used for **15a**. It was isolated as a gum (50%) by means of column chromatography (silica gel, hexane-dichloromathane, 1:9) (Found: C, 68.2; H, 4.4; N, 10.4. $C_{23}H_{18}ClN_3O_2$ requires C, 68.4; H, 4.5; N, 10.4%); $\upsilon_{max.}$ 1730 (C=O), 1610, 1590 (C=N), 885, 880, 850, and 845 cm^{-1} (two 1,4-disubstituted aromatic rings); δ_H 1.14 (3H, t, OCH_2CH_3, $J_{11,12}$ 7.0 Hz), 4.35 (2H, dq, $CH_aH_bCH_3$, $J_{11a,11b}$ 20.0, $J_{11,12}$ 7.0), 6.85 (3H, m, Ar*H*), 7.12 (2H, m, Ar*H*), 7.40 (5H, m, Ar*H*), 7.59 (1H, m, Ar*H*) and 7.88 (2H, m, Ar*H*); δ_C 13.9 (OCH_2CH_3), 66.3 (OCH_2CH_3), 114.5, 119.9, 121.5, 121.6, 123.6, 125.2, 125.6, 127.7, 128.9, 129.1, 131.2, 132.5, 136.6, 142.4, 152.0, 152.2 (aromatic carbon atoms C-9a and C-3), and 175.0 (*C*O); *m/z* 403/405 (M^+), 374/376 (M^+ - CH_2CH_3).

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REFERENCES.

1. *1,3-Dipolar Cycloaddition Chemistry*, Padwa, A. *Ed.*;Wiley-Interscience; New York, **1984** vols 1-2.
2. Huisgen, R.; Grashey, R.; Aufderhaar, E.; Kunz, R. *Chem. Ber.*, **1965**, *98*, 642-649.
3. Rajagopalan, P. *Tetrahedron Lett.*, **1969**, 311-312.
4. Sasaki, T.; Yoshioka, T.; Suzuki, Y. *Bull. Chem. Soc. Jpn.*, **1969**, *42*, 3335-3338.
5. (a) Luheshi, A.-B. N.; Smalley, R. K.; Kennewell, P. D.; Westwood, R. *Tetrahedron Lett.*, **1990**, *31*, 123-126; (b) Luheshi, A.-B. N., Ph.D. Thesis, University of Salford, 1989.
6. Luheshi, A.-B. N.; Smalley, R. K.; Kennewell, P. D.; Westwood, R. *Tetrahedron Lett.*, **1990**, *31*, 127-130.
7. Miller, D. J.; Scrowston, R. M.; Kennewell, P. D.; Westwood, R. *Tetrahedron*, **1992**, *48*, 7703-7712.
8. Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.*, **1976**, *98*, 6397-6399; Caramella, P.; Gandour, R. W.; Hall, J. A.; Deville, C. G.; Houk, K. N. *J. Am. Chem. Soc.*, **1977**, *99*, 385-392; Houk, K. N. *Acc. Chem. Res.*, **1975**, *8*, 361-369.
9. Matoba, K.; Yamazaki, T. *Chem., Pharm. Bull.*, **1974**, *22*, 2999-3001.
10. Anderson, D. R.; Keute, J. S.; Koch, T. H.; Moseley, R. H. *J. Am. Chem. Soc.*, **1977**, *99*, 6332-6340.
11. Hantzsch, A. *Ber.*, **1921**, *54*, 1221-1257.
12. (a) R. K. Smalley, personal communication; (b) S. M. Salem, Ph.D. Thesis, Salford University, 1991; the author prepared two cycloadducts from the reaction of 2-nitro- and 4-methoxy-benzonitrile oxides and 2-methoxy-1*H*-indol-3-one (72 and 64% yield respectively).
13. Huisgen, R. *Angew. Chem., Int. Ed. Engl.*, **1963**, *2*, 565-598.
14. McGillivray, G.; ten Krooden, E., *S. Afr. J. Chem.*, **1986**, *39*, 54-56.
15. Liu, K.-C.; Shelton, B. R.; Howe, R. K. *J. Org. Chem.*, **1980**, *45*, 3916-3918.
16. Levin, N.; Hartung, W. H. *Org. Synth., Coll. Vol. III*, **1955**, 191-193.

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