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2-ISOXAZOLINE DERIVATIVES—VIII[a]

THE REACTION OF NITRILE OXIDES WITH TROPONE

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Abstract—The reaction of nitrile oxides with tropone yields a mixture of at least 8 products, the structures of which are based on spectral and chemical evidence. Both addition of the 1,3-dipole to the carbonyl group and cycloadditions to the C=C double bonds system have been observed. Peri-, regio- and stereo-selectivity of the 1,3-dipole cycloaddition are discussed and rationalized on the basis of simple perturbation theory approach.

Owing to its structure of planar[1] polyenone[2], having ideal electronical and geometrical requisitions for acting as a π_s^2, π_s^4, π_s^6 or π_s^8 component[3], tropone is a suitable substrate for studying periselectivity[4] in cycloadditions.

The reactivity of tropone in 1,3-dipolar cycloadditions has been briefly studied. In the reaction between tropone and diphenylnitrile imine, besides the $[\pi_s^4 + \pi_s^2]$ cycloadduct to the C_2–C_3 double bond Houk[5] isolated for the first time the allowed $[\pi_s^6 + \pi_s^4]$ cycloadduct.

Furthermore the reaction between diazoalkanes and tropone has been investigated by Frank-Neumann[6] and by Houk,[7] who demonstrated that the initially obtained [4 + 2] monoadduct to the C_2–C_3 double bond has a reverse regiochemistry compared with that commonly observed in the cycloadditions of diazoalkanes to α,β-unsaturated ketones.

Pursuing our studies on nitrile oxides, in particular on their cycloaddition to α,β-unsaturated carbonyl compounds,[8] tropone seemed an interesting substrate, suitable to study both the tendency of nitrile oxides to yield a [6 + 4][9] together with a [4 + 2] cycloaddition and the regiochemistry of the latter addition to the tropone C_2–C_3 double bond. Moreover, on the basis of the calculated magnitudes of the frontier orbitals coefficients of tropone[10–12] and of nitrile oxides[13,14] it would be possible to interpret the experimental results in the light of the recently proposed perturbational theory approach to 1,3-dipolar cycloadditions and their regiochemistry.[15,16]

METHODS AND RESULTS

The reactions were carried out in benzene at room temperature in the presence of a large excess of tropone. Mesitonitrile oxide (**1b**) reacted as such, whereas benzonitrile oxide (**1a**) was either generated *in situ* from benzhydroximic acid chloride and Et_3N (Method A) or liberated first from the same reagents (slight excess of Et_3N) and then added to the benzene solution of tropone (Method B). This latter method showed that the formation of the products, in particular of **4a**, was not influenced by the presence of catalytic amounts of acids, due to the excess of benzhydroximic acid chloride, which could *a priori* alter the periselectivity of the cycloaddition.[17]

Tropone (**2**) reacts sluggishly: even with a large excess of **2** the reaction mixture from **1a** contained isolable amounts of the dimer of **1a**, whereas completion of the reaction with **1b** (monitored through TLC) was reached only after 15 days.

The reaction mixtures were very complex; column chromatography allowed isolation and characterisation of products **3–10** with the yields reported in Table 1. Structure assignments are based on chemical and spectroscopical evidence.

Acid hydrolysis to benzamidoxime and benzophenone as well as catalytic hydrogenation to benzophenone allowed structure assignment **4a** to the second eluted reaction product from **1a** and **2**. The structure was confirmed by synthesis from **1a** and benzophenone imine (**27**).

The IR, showing a strained saturated carbonyl group, UV and NMR spectra of the third eluted product are all compatible with structure **5a**, derived from a [6 + 4] cycloaddition of the benzonitrile oxide to the positions 2 and 7 of tropone. Very similar spectral data are reported for the analogous cycloadduct obtained from tropone and diphenylnitrile imine.[5]

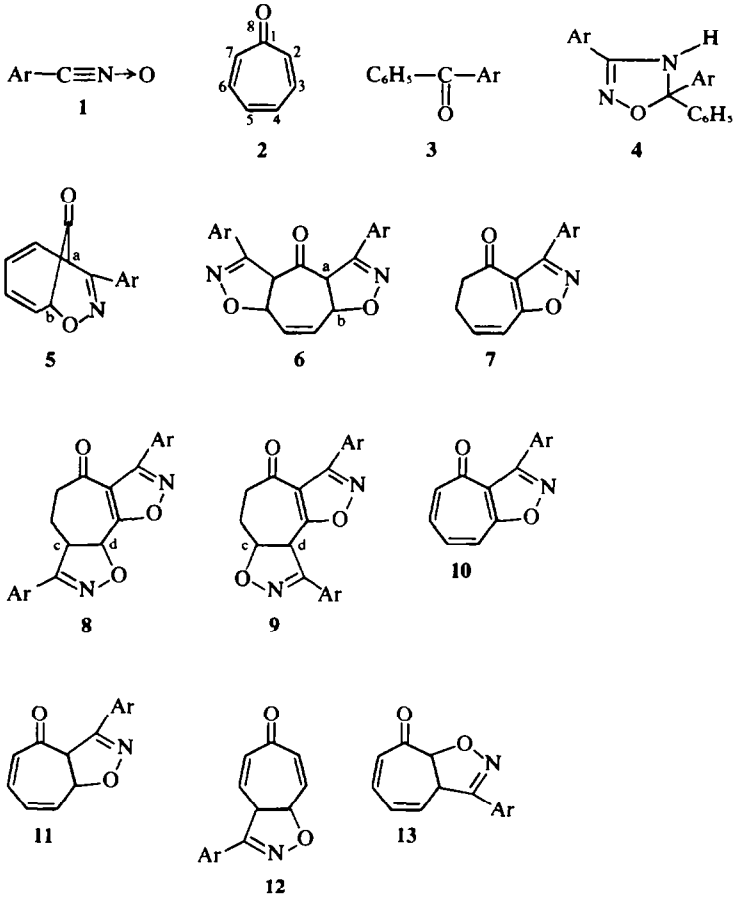
Product **5b** has IR and NMR spectra very similar to **5a**. Its mass spectrum reveals interesting features: besides a very small molecular ion (2% intensity), there are three peaks of high intensity at *m/e* 161 ($C_{10}H_{11}NO^{\cdot+}$, 75%), 106 ($C_7H_6O^{\cdot+}$, 63%) and 78 ($C_6H_6^{\cdot+}$, 100%), whereas all peaks with *m/e* higher than 161 show a low intensity (<4%). The

[a] For Part VII see Ref 18.

Table 1. Yields (%) of the products isolated from the reaction of nitrile oxides with tropone

	3	4	5	6	7	8	9	10
a: Ar = C_6H_5– Method A[a]	18	26	3·5	7·0	7·5	3·5(37)	5·5(31)	5·5
Method B	7·0	47	3·5	trace	3·5	0·5	2·0	4·5
b: Ar = 2,4,6 $Me_3C_6H_2$–[a]	—	—	0·6	2·5[b]	4·0	4·5(7·0)	5·5(72)	57

[a]The bracketted values of **8** and **9** refer to the cycloadditions of **1a** (or **1b**) with **7a** (or **7b**, resp).
[b]Compound **6b** was not isolated as such but as a fully aromatized derivative as demonstrated by IR and NMR data (see Experimental).



a: Ar = C_6H_5
b: Ar = 2,4,6-$Me_3C_6H_2$

SCHEME 1.

cycloadduct **5b** therefore initially undergoes a dipolar retrocycloaddition with charge retention both on the dipole (mesitonitrile oxide)* and on the dipolarophile (tropone). This latter ion thereafter looses CO following its characteristic fragmentation pattern.[3]

*In the mass spectrum of mesitonitrile oxide the molecular ion is also the base peak: our results, unpublished.

The structure of the bis-adduct **6a** was deduced from the IR (saturated carbonyl) and NMR spectrum, which reveals a symmetrical molecule and assigns its regiochemistry, based on the observation that in structurally similar 2-isoxazolines the protons in the 4-position resonate at higher field than the 5-protons. Furthermore the higher-field signal (2H) is a doublet. The failure to yield benzonitrile on treatment with KOH/MeOH confirmed the regiochemistry of both isoxazoline

rings. Indeed, 3-phenyl-5-acylisoxazolines are known to cleave to benzonitrile and α-diketones under basic conditions, whereas the 4-acylisomers are stable or dehydrogenate under the same conditions.[8,18] On steric ground an *anti* stereochemistry can be proposed for cycloadduct **6a**.

The position and the regiochemistry of the isoxazole ring in products **7** and **10** could be deduced from their hydrogenation with the Stork method[19] to yield **14** (Scheme 2). This latter product was also obtained by oxidation of **15**, with chloranil and Et_3N in the case of **15a** whose structure was already known,[8] or directly heating with Et_3N in the case of **15b**. The behaviour of **15b** under basic conditions (dehydrogenation instead of ring cleavage to mesitonitrile and α-cycloheptandione) demonstrates its regiochemistry, further confirmed by NMR data. Furthermore, the absence of NMR signals characteristic for α and β protons of α,β-unsaturated ketones allowed the establishment of the position of the double bond in **7**.

Products **8** and **9** could also be obtained, although rather sluggishly, by further cycloaddition of **7** to **1a** or **1b**. The NMR spectrum of the product with higher R_F value shows quite different chemical shifts for protons c resp. d, in accordance with structure **8**, whereas in **9** very similar chemical shifts are observed for the same protons.

Finally it is important to note that no product having the same regiochemistry as **13** (tropone carbonyl bound to position 5 of the isoxazoline ring) could be evidenced although the complexity of the reaction mixture does not allow exclusion of its presence in minimum amounts. Furthermore, we were unable to isolate the primary adducts **11** or **12**, but only the bis-adducts (derived from **11** or **12**) or some transformation products formed through a dehydrogenation or an internal hydrogen rearrangement.

In order to get some insight into the origin of the bis-adducts **8** and **9**, it would have been useful to compare the dipolarophilic reactivity of the monoadducts **11** and **12**. Since these were not available, we have studied the reaction of **1a** and **1b** with the model compounds **16** and **19**.

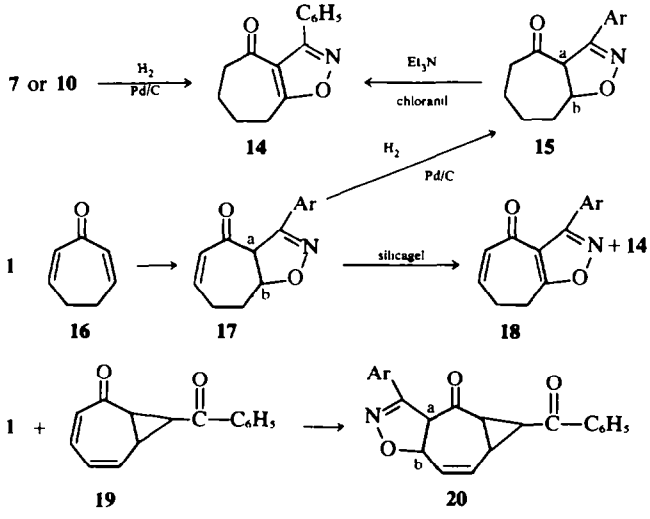
4,5-Dihydrotropone (**16**) readily reacted with **1a** or **1b**, yielding the monoadduct **17**,* which could be selectively hydrogenated to **15**. By silicagel chromatography compound **17b** gave isomer **14b** as the main product through an internal hydrogen transfer, and the dehydrogenated compound **18b** as a minor product, which could in turn be hydrogenated to **14b**.

The reaction of **19** with **1a** or **1b** led to a complex mixture of products, still under examination. Nevertheless, in both cases the main product, isolated in 40–50% yield, has structure **20** as demonstrated by NMR and IR data, as well as by the fact that the compound **20a** did not yield benzonitrile by treatment with KOH/MeOH.

*The crude reaction product from **1a** and **16** gave traces of benzonitrile upon treatment with KOH/MeOH. This fact suggests the presence of small amounts of the regioisomer of **17**, which however we were unable to isolate and characterize otherwise.

DISCUSSION

From the data reported in Table 1 it appears that both benzophenone (**3a**) and the oxadiazoline **4a** are derived from benzophenone imine (**27**), through



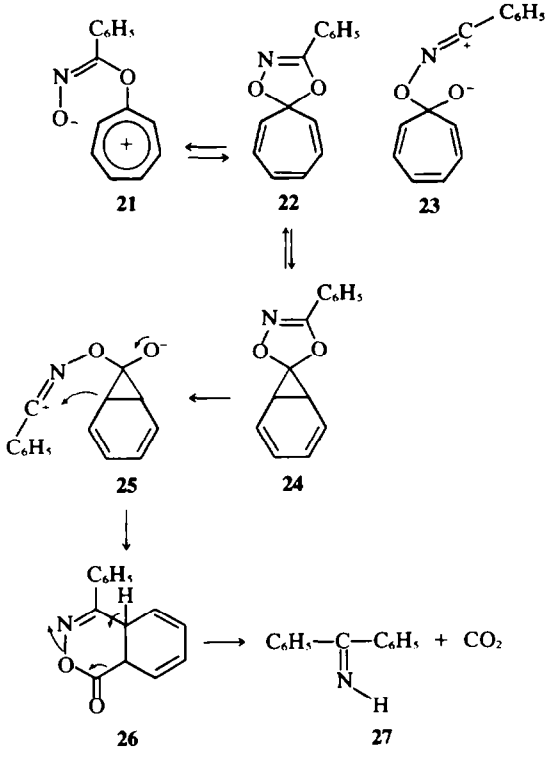
a: Ar = C_6H_5
b: Ar = 2,4,6-$Me_3C_6H_2$

SCHEME 2.

hydrolysis and through cycloaddition with a molecule of benzonitrile oxide, respectively. Furthermore, the different behaviour between **1a** and **1b** cannot be ascribed to a possible acidic catalysis in the reaction of **1a**.

Formation of **27**, in our opinion, is due to an initial nucleophilic attack of the tropone oxygen atom on the nitrile oxide carbon atom to yield **21**.* This intermediate can equilibrate, through **22** and **24**, with **25**, easily rearrangeable to **26**,† which in turn can decompose to CO_2 and **27**. (Scheme 3)

This mechanism is in agreement with the high nucleophilicity of the tropone O atom[3] and with the well-known tendency of the nitrile oxide C atom to react with nucleophiles[23] as well as with the cycloheptatriene/norcaradiene tautomerism and with the facile base-induced rearrangement of tropone homologs to benzene derivatives.[3]



SCHEME 3.

Consistent with the proposed mechanism, mesitonitrile oxide (**1b**), which is less prone toward nucleophilic attack both for steric and electronic factors, did not react with the tropone carbonyl. By the way, this fact definitely excludes the intermediacy of **23**. A concerted process, leading directly to **22**, seems less probable, also in consideration of simple frontier-orbitals arguments, as below observed.

In the case of the cycloadducts formed by addition to the C=C double bonds, the behaviour of nitrile oxides seems different from that of nitrile imines[5]‡ and diazoalkanes,[6,7] which react only with the C_2–C_3 double bond of tropone and not at all with the C_4–C_5 double bond. As a matter of fact, bis-adducts **8** and **9** are probably derived from the monoadduct **12**, not isolated, for the following reasons: (i) compound **7** is not very reactive and adds nitrile oxides **1** to yield a ratio **8**/**9** different from the ratio obtained directly from **1** and **2**; (ii) the model compound **19** (comparable with **11**) reacts with **1** to yield **20** as the main product, in contrast with the results obtained from **1b** and **2**; (iii) the model compound **16** (comparable with **12**) is highly reactive toward nitrile oxides and yields **17**, having the same regiochemistry as **8** and **9**.

The cycloaddition of tropone to both benzo- and mesito-nitrile oxide is regiospecific and periselective, but the periselectivity is greater with **1b** than with **1a**. In the latter case, especially using method B, the cycloaddition [6 + 4] substantially competes with cycloaddition [4 + 2].

The perturbation theory approach, based on a simple frontier orbital model, has been recently used to account for both regio- and peri-selectivity in 1,3-dipolar cycloaddition reactions.[15,16] The interaction energy[24] between the two cycloaddends schematically depends on three parameters, which control the preferential formation of one or the other isomer. That regio-(peri)isomer will be favoured which allows: (i) the interaction between the centers having the largest and the smallest coefficient on the cycloaddends HOMOs (closed repulsion shell term); (ii) the best electrostatic interaction between the net charges of the interacting centers (coulombic term); (iii) the combination of the largest coefficients on the HOMO/LUMO pair, having the lowest energy difference (overlap or charge transfer stabilization term). A qualitative rationalization of the regio- and peri-selectivity in all 1,3-dipolar cycloadditions was substantially based on this latter term.[15,16]

A close inspection of Table 2, which collects some literature data on the frontier orbitals of tropone and benzonitrile oxide, reveals that the overlap stabilization term, whatever the preferred

*Analogous zwitterions have been proposed in the cycloadditions of tropone to sulphenes[20], ketenes and sulphonyl isocyanate.[21] Furthermore a zwitterionic intermediate, in competition with the concerted process, must be invoked to explain the formation of acetylenic oximes besides isoxazoles in the reaction of nitrile oxides with monosubstituted alkynes.[22]

†Of course a direct formation of **26** from **24** cannot be excluded *a priori*, although a concerted $[\sigma_s^2 + \sigma_s^2]$ process seems unlikely because of steric hindrance.

‡As a matter of fact, nitrile imines react both with double bond C_2–C_3, yielding the two possible regioisomers, and with double bond C_4–C_5 $\left(\text{ratio } \frac{C_2\text{–}C_3}{C_4\text{–}C_5} \simeq 13\right)$: our results, unpublished.

Table 2. Coefficients[a], energies[b] of the frontier MOs and total charges[c] for tropone and benzonitrile oxide

	Tropone							Benzonitrile oxide				
	c_8	c_1	c_2	c_3	c_4	β	(eV)	c_C	c_N	c_O	β	(eV)
LUMO[d]	—	—	0·521	−0·232	−0·418	−0·44	(−2·61)	0·326	−0·477	0·253	−0·45	(2·19)
HUMO[d]	0·653	−0·187	−0·393	−0·093	0·326	0·71	(−9·46)	0·438	0·308	−0·602	0·85	(−11·02)
Total charges[d]	−0·298	0·246	−0·038	0·039	0·016			−0·07	0·21	−0·41		

[a]The reported coefficients derive from Hückel calculations for the tropone[10] and by CNDO/2 calculation for the benzonitrile oxide.[13]

[b]The reported energies in β are calculated by Hückel method both for tropone[10] and for benzonitrile oxide[14], whereas values in eV are calculated by CNDO/2 method for benzonitrile oxide[13] and by SCF π-electron method for tropone[12].

[c]Calculated by CNDO/2 method for both molecules.[2,13]

[d]Owing to the symmetry of the tropone molecule, coefficients c_5, c_6 and c_7 are equal to c_4, c_3 and c_2, respectively, for the HOMO, and to $-c_4$, $-c_3$, $-c_2$, respectively, for the LUMO. Total charges on C_5, C_6, C_7 are equal to C_4, C_3 and C_2, respectively.

HOMO/LUMO interaction may be, would indicate a predominance of the [6+4] cycloadduct, i.e. of isomer **5**, over both monoadduct **11** and monoadduct **13**.

Therefore, in our case the third term of the simple "frontier" orbitals approach alone seems inadequate to explain the observed periselectivity, which definitely shows a preponderance of the [4+2] cycloadducts over the [6+4] adduct. This reversal of periselectivity may be caused by several factors. First of all, both the closed repulsion shell term and the Coulombic term favour isomer **11** with respect to monoadducts **5** and **13**. Secondly, a dipole-dipole interaction cannot *a priori* be neglected, owing to the relatively high dipole moments of the two addends (μ = 4·00 D for **1a** and 4·41 D for **1b**, μ = 4·30 D for tropone). From this point of view the orientation complex leading to **11** is favoured over the ones leading to **5** or to **13**. Finally, the stability of the product can influence the transition state. Although the distance C_2–C_7 (≃ 2·55 Å) of tropone is suitable for attack from a linear molecule of nitrile oxide (C–N–O length ≃ 2·40 Å), the adduct **5** is possibly less stable (strained ring and absence of conjugation between the diene system and carbonyl group) than **11**. Moreover, the higher periselectivity of **1b** than **1a** suggests a higher steric demand of the [6+4] cycloaddition compared with the [4+2] cycloaddition.

Since no experimental values† of frontier orbital energies are known for tropone or nitrile oxides and since energy values obtained from semiempirical calculations are not completely reliable, it is difficult to deduce which HOMO-LUMO interaction prevails in this case. However, the regiospecificity of the reaction and the remark that all calculation methods used (Hückel, SCF π-electron, CNDO/2) led for both tropone[7,10–12] and benzonitrile oxide[13,14] to the same coefficient pattern, would indicate a predominant HOMO (tropone)-LUMO (nitrile oxide) interaction. In this case indeed the third term as well favours the regioisomer **11**.

The regiochemistry of **11** is opposite to that observed in the cycloadducts from nitrile oxides and simple α,β-unsaturated carbonyl compounds (acrylic aldehyde, methyl acrylate, methylvinylketone), where a preferential HOMO (dipolarophile)-LUMO (dipole) interaction has likewise been inferred.[15,16,25] This reversal of regioselectivity agrees well with the reversed relative magnitudes of α- and β-coefficients on the HOMOs of tropone and α,β-unsaturated ketones respectively.[13]*

Finally, it should be noted that, whereas the LUMO coefficients on the reactive centers of the benzonitrile oxide have the same sign, the HOMO coefficients on the tropone carbonyl atoms show opposite signs. This fact should make a concerted cycloaddition of the nitrile oxide to the C=O double bond unlikely, and, together with the stability of the tropylium ion, should favour an initial formation of the dipolar intermediate **21**.

EXPERIMENTAL

M.ps are uncorrected. UV spectra were obtained as absolute EtOH solutions on a Perkin Elmer 137 recording instrument and IR spectra as Nujol suspensions on a Perkin Elmer 257 spectrophotomer. The NMR spectra (60 MHz) were recorded at 36° on a Perkin Elmer R 12 spectrometer with TMS as internal standard for $CDCl_3$ solutions by Dr. A. Gamba Invernizzi.

TLC was performed on plates precoated with silica gel GF_{254} (Merck). In some cases the products were detected on TLC plates with a 3% soln of CrO_3 in 50% H_2SO_4 followed by heating at 120° in an air bath.

Preparative columns were prepared with silica gel H (Merck) and eluted with cyclohexane/AcOEt mixtures in various proportions unless otherwise stated.

The identity of compounds was always established with the aid of authentic material by mixed m.p. determination and by comparison of IR spectra and R_F values (TLC).

Elemental analysis were performed by Dr. L. Maggi Dacrema.

Physical, analytical and IR data are given in Table 3.

Reaction of benzonitrile oxide (**1a**) *with tropone* (**2**)

Method A. A stirred soln of benzhydroximic acid chloride (2·70 g, 17·4 mmoles) and a large excess of tropone[26] (18·0 g, 170 mmoles) in anhyd benzene (60 ml) was treated with a soln in the same solvent (30 ml) of the stoichiometric amount of triethylamine, added dropwise at room temp during 7 hr. The resulting mixture was left aside for 48 hr. The precipitated $Et_3N{\cdot}HCl$ was filtered off and the soln washed several times with water to remove the unreacted tropone and dried.

The solvent was evaporated under reduced pressure and the residue was separated by column chromatography to give, in order of elution, 3,4 - diphenylfurazane - N - oxide (11%) and compounds **3a–10a**. Yields of compounds **3a–10a** are given in Table 1.

Compound **4a**, colourless needles from EtOH m.p. 176–178°, was identical in every respect with the adduct of benzonitriloxide to benzophenonimine.[27]

A bisadduct, whose spot on TLC was running between that of **4a** and **5a**, was also isolated (2·5%) and purified as slight brown needles from EtOH m.p. 169–171° dec. (Found: C, 73·3; H, 4·9; N, 8·5. Calc. for $C_{21}H_{16}N_2O_3$: C, 73·2; H, 4·7; N, 8·1%). This compound, with a satured carbonyl (1728 cm^{-1}), showed a complex NMR spectrum and on treatment with NaOH/EtOH did not give benzonitrile (odour). This structure was not further studied.

Other products were isolated in small amount but not characterized.

NMR and UV data of compounds **5a–10a**. **5a**: λ_{max} 241 nm (log ϵ 4·18); δ 4·34 (1H, m, H-a, J = 8·0 and

*The regiochemistry of **11** is, however, the same as for the cycloadducts obtained from nitrile oxides and cyclic α,β-unsaturated ketones. This observation will be discussed elsewhere shortly.

†*Note added in proof*: The recently measured vertical IP of tropone (8·90 eV) is consistent with the proposed HOMO (tropone)–LUMO (nitrile oxide) predominant interaction: J. C. Bünzli, D. C. Frost and C. Weiler, *J. Am. Chem. Soc.* **96**, 1952 (1974).

Table 3. Characterization data of compounds **5–20**

Comp.	M.p.°C	Recrystall. solvent	Found % C	H	N	Elemental analyses Formula	Calc. % C	H	N	ν_{max}/cm^{-1} (C=O)
5a	140–1	Petrol ether[a]	74·7	5·1	6·3	$C_{14}H_{11}NO_2$	74·7	4·9	6·2	1756
5b	107–11	—	—	—	—	$C_{17}H_{17}NO_2$	—	—	—	1743
6a	217 dec.	Benzene[b]	73·5	4·9	8·0	$C_{21}H_{16}N_2O_3$	73·2	4·7	8·1	1732
7a	90–2	Petrol ether[a]	75·2	5·1	6·3	$C_{14}H_{11}NO_2$	74·7	4·9	6·2	1678
7b	118–9	MeOH[c]	76·4	6·6	5·2	$C_{17}H_{17}NO_2$	76·4	6·4	5·2	1670
8a	211–2	EtOH[c]	72·9	4·8	8·3	$C_{21}H_{16}N_2O_3$	73·2	4·7	8·1	1686
8b	198–200	EtOH[d]	76·0	6·6	6·8	$C_{27}H_{28}N_2O_3$	75·7	6·6	6·5	1672
9a	180–3	EtOH[c]	73·2	4·8	8·1	$C_{21}H_{16}N_2O_3$	73·2	4·7	8·1	1682
9b	195–7	EtOH[b]	75·6	6·5	6·7	$C_{27}H_{28}N_2O_3$	75·7	6·6	6·5	1679
10a	145–8	EtOH[a]	75·4	4·2	6·3	$C_{14}H_9NO_2$	75·3	4·1	6·3	1640, 1607
10b	134–5	EtOH[a]	76·5	5·6	5·5	$C_{17}H_{15}NO_2$	77·0	5·7	5·3	1640, 1610
14a	94–5	Cyclohexane[d]	74·5	5·8	6·1	$C_{14}H_{13}NO_2$	74·0	5·8	6·2	1670
14b	80–2	Petrol ether[a]	75·6	7·1	5·3	$C_{17}H_{19}NO_2$	75·8	7·1	5·2	1668
15b	86–7	Petrol ether[b]	74·8	7·8	5·2	$C_{17}H_{21}NO_2$	75·2	7·8	5·2	1712
17a	118–21	EtOH[b]	74·1	5·9	6·2	$C_{14}H_{13}NO_2$	74·0	5·8	6·2	1680
17b	106–8	Cyclohexane[b]	75·4	7·2	5·3	$C_{17}H_{19}NO_2$	75·8	7·1	5·2	1668
18b	138–141	MeOH[c]	76·6	6·7	5·2	$C_{17}H_{17}NO_2$	76·4	6·4	5·2	1645
20a	213–5	EtOH[b]	77·1	5·2	4·1	$C_{22}H_{17}NO_3$	77·0	5·0	4·1	1720, 1671
20b	183–5	EtOH[b]	77·9	5·9	3·6	$C_{25}H_{23}NO_3$	77·9	6·0	3·6	1710, 1663

[a]Prisms. [b]Needles. [c]Platelets. [d]Leaflets.

2·0 Hz), 4·90 (1H, m, H-b, J = 5·7 and 2·0 Hz), 5·50–6·50 (4H, m, vinyl protons). **6a**: δ 4·78 (2H, d, H-a, J_{ab} = 10·0 Hz), 5·48 (2H, m, H-b), 6·28 (2H, m, vinyl protons). **7a**: δ 2·66 (4H, m, $-CH_2-CH_2-$) 6·69 (2H, m, vinyl protons). **8a**: δ 1·90–2·10 (2H, m, $-CH_2-CH<$), 2·42–2·77 (2H, m, $-CH_2-CO-$), 3·80–4·50 (1H, m, H-c), 5·92 (1H, d, H-d, J_{cd} = 10·0 Hz). **9a**: δ 2·00–2·50 (2H, m, $-CH_2-CH$), 2·60–2·98 (2H, m, $-CH_2-CO-$), 5·30 (1H, m, H-c), 5·52 (1H, d, H-d, J_{cd} = 11·5 Hz). **10a**: λ_{max} 225 nm (log ε = 4·41); δ 6·80–7·20 (3H, m), 7·30–7·90 (6H, m).

Compound **6a** on treatment with NaOH/EtOH did not give benzonitrile (odour).

Method B. To a stirred soln of benzhydroximic acid chloride (1·20 g, 7·7 mmoles) in anhyd benzene (30 ml) cooled to 0° a slight excess of triethylamine was added. After 15 min the precipitated $Et_3N{\cdot}HCl$ was filtered off and to the resulting soln a large excess of tropone (10·0 g, 94·5 mmoles, dissolved in benzene) was added. The mixture was left at room temp for 48 hr and then worked up as described in Method A to give 3,4 - diphenyl - furazane - N - oxide (13%) and compounds **3a–10a**. (Yields are given in Table 1).

Small amounts of unknown products were also isolated.

Adducts **5a–10a** are stable in the reaction and work-up conditions.

Reaction of mesitonitrile oxide (**1b**) *with tropone* (**2**). A soln of mesitonitrile oxide (3·00 g, 18·6 mmoles) and a large excess of tropone (10·0 g, 94·5 mmoles) in anhyd benzene (70 ml) was left at room temp for 15 days until total disappearance of the dipole (by monitoring through TLC). The unreacted tropone was removed by extraction with water and the solution dried, filtered and evaporated under reduced pressure. The resulting residue was chromatographed on a column to give in order of elution: mesitonitrile (traces), a solid product (63 mg) not further characterized, and a product (93 mg, 2·5%) purified by crystallization as colourless needles from EtOH m.p. 245–7° (Found: C, 76·8; H, 5·6; N, 6·5. Calc. for $C_{27}H_{24}O_3N_2$: C, 76·4; H, 5·7; N, 6·6%); ν_{max}: 1635 cm^{-1} (C=O), δ 1·90 (12 H, s, o-Me), 2·15 (6H, s, p-Me), 6·91 (4H, bs, aromatic protons), 8·05 (2H, s, tropone ring protons). NMR data show that the structure of this latter product is symmetrical and fully aromatic (the 4 isoxazolinic protons are lacking).

5b: δ 4·02 (1H, m, H-a, J = 8·5 and 2·3 Hz), 4·92 (1H, m, H-b, J = 6·0 and 2·3 Hz), 5·30–6·50 (4H, m, vinyl protons). **8b**: δ 3·65–4·15 (1H, m, H-c), 5·95 (1H, d, H-d, J_{cd} = 9·3 Hz). **7b**: δ 2·60 (4H, m, $-CH_2-CH_2-$), δ 6·73 (2H, m, vinyl protons). **9b**: δ 5·38 (2H, m, H-c and H-d). **10b**: δ 6·80–7·30 (6H, m); λ_{max} 230 nm (shoulder, log ε = 4·37).

Yields of compounds **5b–10b**, which are stable in the reaction and work up conditions, are given in Table 1.

Catalytic hydrogenation of **4a**. A soln of **4a** (137 mg) in EtOH (95%; 10 ml) was hydrogenated over 10% Pd-C (15 mg) catalyst under atmospheric pressure (760 Torr) and at room temp. One equivalent of H_2 was absorbed. The soln was filtered, poured into water (pH acid) and extracted with ether. The ether extracts were dried and evaporated to give **3a** (80 mg, 95%).

Hydrolytic cleavage of **4a**. A soln of **4a** (300 mg) and 0·2 ml of 36% HCl in EtOH (95%; 10 ml) was heated under reflux for 6 hr. After cooling the mixture was poured into water and extracted with ether to give, after usual work up, a quantitative yield of **3a**. The aqueous soln was basified (Na_2CO_3) and extracted with ether to give benzamidoxime (120 mg, 87%).

Catalytic hydrogenation of compounds **7**, **10**, **17** *and* **18**. Compounds **7**, resp. **10**, **17** and **18** (300 mg) were dissolved in ACOEt/ACOH (4:1; 30 ml) and catalytically reduced with H_2 and Pd/C 5% (30 mg) under normal pressure (760 Torr) and at room temp. After an uptake of 1·1 (2·2 in the case of **10a** and **10b**) equivalent of H_2 the reaction was interrupted, the soln filtered and the solvent evaporated under reduced pressure. The crude products were purified by column chromatography or by crystallization from appropriate solvent to give ≈90–95% yields of pure **14** or **15**. NMR data of **15b**: δ 4·47 (1H, d, H-a), 4·97 (1H, m, H-b).

The hydrogenation of **7b** and **10b** under the same conditions was carried out without interruption until no more H_2 was absorbed (2·1 and 3·2 equiv for **7b** resp. **10b**).

After usual work up a new compound was isolated (quantitative yield) as colourless needles from EtOH m.p. 218–9° (Found: C, 74·8; H, 7·8; N, 5·3. Calc. for $C_{17}H_{21}NO_2$: C, 75·2; H, 7·8; N, 5·2%).

Reaction of benzonitrile oxide (**1a**) *with* **7a**, **16** *and* **19**

(a) To a stirred solution of **7a** (116 mg, 0·52 mmoles) and benzhydroximic acid chloride (90 mg, 0·58 mmoles) in anhyd benzene was added dropwise the stoichiometric amount of triethylamine in the same solvent during 4 hr at room temp. The mixture was then left aside for 48 hr. The Et_3NHCl was filtered off and the solvent evaporated under reduced pressure to give a residue that during chromatography gave 3,4 - diphenylfurazane - N - oxide (26 mg), some unreacted **7a** (44 mg), **8a** (41 mg, 37%) and **9a** (34 mg, 31%).

(b) The benzonitrile oxide was slowly liberated in anhyd benzene as in (a) in the presence of **16**[28] (30% excess). TLC analysis showed that 3,4 - diphenylfurazane - N - oxide was not present in the mixture. Usual work up and crystallization of the crude product from cyclohexane gave pure **17a** (91%). The residue from evaporation of the mother liquors, on treatment with NaOH/EtOH, gave benzonitrile odour, but no signals consistent with the presence of the regioisomer of **17a** were detected in its NMR spectrum. NMR data of **17a**: δ 4·82 (1H, d, H-a, J_{ab} = 12·0 Hz), 5·18 (1H, m, H-b), 5·83 (1H, m, =CH–CO–), 6·52 (1H, m, =CH–CH_2–).

(c) The benzonitrile oxide (20% excess) was slowly liberated in anhydrous benzene as in (a) in the presence of **19**[29]. After usual work up the resulting residue was treated with EtOH to give **20a** (260 mg). The mother liquors were evaporated and chromatographed to give 3,4 - diphenylfurazane - N - oxide, some more **20a** (25 mg, overall yield 46%) and minor amounts of other compounds which are under study. Compound **20a** on treatment with NaOH/EtOH did not give benzonitrile (odour).

NMR data of **20a**: δ 5·03 (1H, d, H-a, J_{ab} = 11·0 Hz), 5·43 (1H, m, H-b), 6·07 (2H, m, vinyl protons).

Reaction of mesitonitrile oxide (**1b**) *with* **7b**, **16** *and* **19**

(a) A soln of **7b** (105 mg, 0·33 mmoles) and of mesitonitrile oxide (100 mg, 0·62 mmoles) in anhyd benzene (5 ml) was left at room temp until TLC analysis showed the total disappearance of **7b** (30 days). Then the solvent was evaporated and the residue chromatographed to give **8a** (12 mg, 7%), **9a** (121 mg, 72%) and 25 mg of a compound which was not further studied.

A parallel experiment in benzene/MeCOMe 1:1 gave the same results.

(b) The reaction of mesitonitrile oxide (1·10 g, 6·9 mmoles) with **16** (1·00 g, 9·3 mmoles) went to completion after 24 hr as shown by TLC analysis. The solvent was evaporated and the residue crystallized from cyclohexane to give pure **17b** (1·52 g, 83%). The NMR spectrum of the oily product obtained from evaporation of the mother liquors is consistent with a mixture of **17b** and **16**.

In a duplicate experiment the reaction residue was chromatographed on silicagel H (merck) (eluant benzene/AcOEt 9:1) to give **14b** (82%) and **18b** (13%).

NMR data of **17b**: δ 4·88 (1H, d, H-a, J_{ab} = 12·0 Hz), 5·20 (1H, m, H-b), 5·83 (1H, m, =CH–CO–), 6·60 (1H, m, =CH–CH_2–).

(c) A soln of mesitonitrile oxide (161 mg, 1·00 mmoles) and **19** (240 mg, 1·07 mmoles) in anhyd benzene (6 ml) was left at room temp for 17 days; after that TLC analysis showed the total disappearance of the dipole. Usual work up and chromatography gave **20b** (92 mg, 24%) and 70 mg (18%) of a solid non crystalline product (not further purified) with higher R_F (eluant cyclohexane/AcOEt 4:1) than that of **20b**. This latter product was slowly formed from standing of **20b** in $CHCl_3$ soln; its IR spectrum did not show any absorption due to satured carbonyl [ν_{max}: 1663 cm^{-1} (conjugated CO and PhCO)]; NMR signals due to H-a and H-b were not detected.

Minor amounts of other products were isolated but not characterized.

NMR data of **20b**: δ 4·93 (1H, d, H-a, J_{ab} = 11·3 Hz), 5·52 (1H, m, H-b), 6·03 (2H, m, vinyl protons).

Dehydrogenation of **15a** *with chloranil and triethylamine.* A soln of **15a** (100 mg), chloranil (110 mg) and triethylamine (1 ml) in anhyd benzene was heated under reflux for 24 hr. The ppt was filtered off and the resulting dark-brown soln was treated with decolourising charcoal, filtered and evaporated to dryness. The residue was crystallized from cyclohexane to give **14a** (29 mg, 29%).

In a duplicate experiment the crude product was purified by column chromatography to give **14a** in 80% yield.

Dehydrogenation of **15b** *with triethylamine.* A soln of **15b** (100 mg) and Et_3N (1 ml) in anhyd benzene (5 ml) was heated under reflux for 15 days. Usual work up and chromatography gave **14b** (70 mg).

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REFERENCES

[1]M. J. Barrow, O. S. Mills and G. Filippini, *J.C.S. Chem. Comm.* 66 (1973)
[2]D. J. Bertelli and T. G. Andrews, jr., *J. Am. Chem. Soc.* **91**, 5280 (1969)
[3]F. Pietra, *Chem. Rev.* **73**, 293 (1973)
[4]K. N. Houk, L. J. Luskus and N. S. Bhacca, *J. Am. Chem. Soc.* **92**, 6392 (1970)
[5]K. N. Houk and C. R. Watts, *Tetrahedron Letters* 4025 (1970)
[6]M. Franck-Neumann, *Ibid.* 2143 (1970)
[7]L. J. Luskus and K. N. Houk, *Ibid.*, 1925 (1972)
[8]G. Bianchi, C. De Micheli, R. Gandolfi, P. Grünanger, P. Vita Finzi and O. Vajna de Pava, *J.C.S. Perkin I*, 1148 (1973)
[9]P. Caramella, P. Frattini and P. Grünanger, *Tetrahedron Letters* 3817 (1971)
[10]L. Salem, *J. Am. Chem. Soc.* **90**, 553 (1968)
[11]A. July and M. Bonnet, *Tetrahedron* **20**, 2243 (1964)
[12]H. Kuroda and T. Kunii, *Theor. Chim. Acta* **7**, 220 (1967)
[13]K. N. Houk, J. Sims, R. E. Duke, jr., R. W. Strozier and J. K. George, *J. Am. Chem. Soc.* **95**, 7287 (1973)
[14]M. Yamakawa, T. Kubota, H. Akazawa, L. Tanaka, *Bull. Chem. Soc. Japan* **41**, 1046 (1968)
[15a]K. N. Houk, *J. Am. Chem. Soc.* **94**, 8953 (1972); [b]K. N. Houk, J. Sims, C. R. Watts and L. J. Luskus, *Ibid.*, **95**, 7301 (1973)
[16a]J. Bastide, N. El Ghandour and O. Henri-Rousseau, *Tetrahedron Letters* 4225 (1972); [b]J. Bastide, N. El Ghandour and O. Henri-Rousseau, *Bull. Soc. Chim. Fr.* 2290 (1973); [c]J. Bastide and O. Henri-Rousseau, *Ibid.*, 2294 (1973)
[17]S. Ito, K. Sakan and Y. Fujise, *Tetrahedron Letters* 2873 (1970)

[18]G. Bianchi, A. Gamba Invernizzi and R. Gandolfi, *J.C.S. Perkin I*, in press
[19a]G. Stork, S. Danishefsky and M. Ohashi, *J. Am. Chem. Soc.* **89**, 5459 (1967); [b]G. Bianchi, R. Gandolfi and P. Grünanger, *Tetrahedron*, **26**, 5113 (1970)
[20]A. E. Truce and Cheng-I. M. Lin, *J. Am. Chem. Soc.* **95**, 4426 (1973)
[21]R. Gompper, A. Studeneer and W. Elser, *Tetrahedron Letters* 1019 (1968)
[22a]S. Morrocchi, A. Ricca, A. Zanarotti, G. Bianchi, R. Gandolfi and P. Grünanger, *Ibid.*, 3329 (1969); [b]R. Huisgen, private communication
[23]Ch. Grundmann and P. Grünanger, The Nitrile Oxides, Springer Verlag, Berlin (1971)
[24]L. Salem, *J. Am. Chem. Soc.* **90**, 543 (1968); *Ibid.* **91**, 3793 (1969)
[25]M. Christl and R. Huisgen, *Chem. Ber.* **106**, 3345 (1973)
[26]G. Jones, *J. Chem. Soc.* (C), 1230 (1970)
[27]S. Morrocchi, A. Ricca and L. Velo, *Chim. Ind. Milan* **49**, 168 (1967)
[28]E. W. Garbisch, jr., *J. Org. Chem.* **30**, 2109 (1965)
[29]Y. Sugimura and N. Soma, *Tetrahedron Letters* 1721 (1970)