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Reaction of Azomethine *N*-Oxides. III.[1] Reactions of Some Azomethine *N*-Oxides with Fluoranil, Phenyl Vinyl Sulfone, and β-Nitrostyrene

Ahmed Moukhtar Nour El-Din
Chemistry Department, Faculty of Science, El-Minia University, El-Minia, Egypt
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Isomerization of 3*H*-indole 1-oxides in the presence of tetrafluoro-2,5-cyclohexadiene-1,4-dione (fluoranil) to the thermodynamically more stable lactams was found to proceed via formation of charge-transfer complexes. However, addition of fluoranil to some open chain nitrones did not give the corresponding amides. Both electron-deficient β-nitrostyrene and phenyl vinyl sulfone did not form charge-transfer complexes with nitrones, but instead they undergo 1,3-dipolar cycloaddition giving 4- or 5-substituted isoxazolidines.

Döpp et al.[2,3] have shown that electron-deficient nitriles, ethentetracarbonitrile (TCNE) or oxiranetetracarbonitrile (TCNO) accelerate isomerization of the 3*H*-indole 1-oxide (**1a**) into the lactam (**3a**). Two reaction pathways for this isomerization were postulated.[2,3] The first is the cycloaddition of the nitrone (**1a**) with the cyano group of TCNE or TCNO, followed by fission of the cycloadduct and 1, 2-oxygen migration. The second is the complexation of the 3*H*-indole 1-oxide (**1a**) with the electron-deficient compounds followed by oxygen and hydrogen atoms shifts.[3]

We have recently reported[4–6] that nitrones form charge-transfer complexes with various electron-deficient compounds such as TCNE and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ). This result has urged us to investigate[2,3] about formation and chemical behavior of the complexes between the 3*H*-indole 1-oxides (**1a,b**) and the electron-deficient fluoranil (**2**), together with some analogous reaction systems.

Additions of **1a** and **1b** to equimolar quantities of fluoranil (**2**) in dichloromethane at room temperature have given rise to greenish orange colored solutions, which show two absorption shoulders in the visible region at λ_{max} 490 and 505 nm for **1a** and **1b**, respectively (Table 1). These two absorptions are due to complexation[4–6] between each of the 3*H*-indole 1-oxides (**1a** or **1b**), and the electron-deficient fluoranil. The decomposition of the charge-transfer complexes by heating has led to the thermodynamically more stable lactams (**3a,b**).[7,8] The structures of the lactams (**3a,b**) were varified by both the relevant physical and spectrometric data given in Tables 1 and 2. This result implies that the formation of the charge-transfer complexes between each of 3*H*-indole 1-oxides (**1a,b**) and fluoranil is the first step in the isomerization of **1a** and **1b** to the lactams (**3a,b**). Since the fluoranil does not contain any cyano group, the suggestion[2,3] of the cycloaddition of the 3*H*-indole 1-oxides (**1a,b**) with cyano group in the electron-deficient nitrile compounds can be ruled out. Instead, the too fast isomerization[2] of the 3*H*-indole 1-oxide (**1a**) into the lactam (**3a**) in the presence of TCNE can be attributed to the higher electron affinity of the TCNE compared with that of fluoranil.[9]

The formation of the lactams (**3a,b**) are likely to take place via formation of charge-transfer complexes (**4a,b**) and removal of one electron out of the highest occupied molecular orbital (HOMO) of the 3*H*-indole 1-oxides (**1a,b**). Such an electron transfer facilitates the migration of the oxygen atom from the nitrogen atom to the α-carbon atom, which is followed by an 1,2-hydrogen shift and additional bond reorganization (Fig. 1).

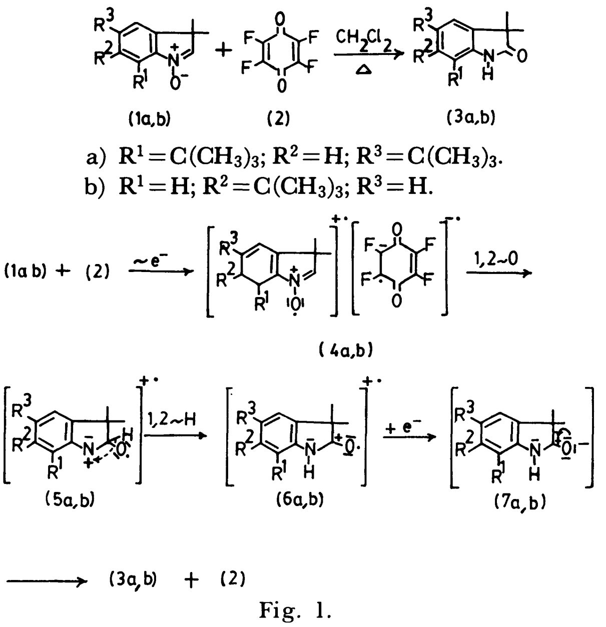
On addition of equimolar quantity of the pyrrole 1-oxide (**12**) to fluoranil in dichloromethane, a pale yellow color developed, and no band for charge-transfer complex was observed in the spectra of the pale yellow solution obtained. Heating of this mixture did not lead to the formation of the corresponding lactam, instead the starting compounds **12** and **2** were recovered. This result reinforces the suggestion that, the rearrangement of the indole 1-oxides (**1a,b**) to lactams (**3a,b**) proceeds via charge-transfer complex formation.

Table 1. Maximum Absorption Wavelengths λ_{max}/nm of Change-Transfer Complexes Formed between the Nitrones (**1a**, **b**; **8a**, **b**, **c**, **d**) and Tetrafluoro-2,5-cyclohexadiene-1,4-dione (**2**) in Dichloromethane at 25 °C

Nitrone	UV-VIS absorption band λ/nm
5,7-Di-*t*-butyl-3,3-dimethyl-3*H*-indole 1-Oxide (**1a**)	490 sh
3,3-Dimethyl-6-*t*-butyl-3*H*-indole 1-Oxide (**1b**)	505 sh
N-(2-Methylbenzylidene)aniline *N*-Oxide (**8a**)	482 sh
N-(3-Methylbenzylidene)aniline *N*-Oxide (**8b**)	475 sh
N-(2,4-Dimethoxybenzylidene)aniline *N*-Oxide (**8d**)	498
N-(3,4-Dimethoxybenzylidene)aniline *N*-Oxide (**8e**)	491

Table 2. Physical and Analytical Data of the Reaction Products of Nitrones (**1a**, **b**), (**8a**—**c**), and (**12**) with Tetrafluoro-2,5-cyclohexadiene-1,4-dione, β-Nitrostyrene and Phenyl Vinyl Sulfone

Compound	Yield	Mp (θ_m/°C)	Mol formula	Found (Calcd) (%)		
	%	(Recryst. from)		C	H	N
5,7-Di-*t*-butyl-3,3-dimethyl-2-indolinone (**3a**)[7]	88	240—241 (Ethanol)	$C_{18}H_{27}NO$	79.18 (79.07	9.90 9.95	5.26 5.12)
3,3-Dimethyl-6-*t*-butyl-2-indolinone (**3b**)[8]	72	195—196 (Cyclohexane)	$C_{14}H_{19}NO$	77.51 (77.38	8.87 8.81	6.40 6.45)
N-(2,4-Dimethoxybenzylidene)aniline *N*-Oxide (**8d**)	69	84—86 (Benzene–hexane)	$C_{15}H_{15}NO_3$	70.21 (70.02	5.75 5.88	5.31 5.45)
N-(3,4-Dimetoxybenzylidene)aniline *N*-Oxide (**8e**)	62	74—76 (Ethanol–hexane)	$C_{15}H_{15}NO_3$	70.12 (70.02	5.76 5.88	5.34 5.45)
2,5-Diphenyl-3-(2-methylphenyl)-4-nitroisoxazolidine (**10a**)	85	75—76 (Ethanol)	$C_{22}H_{20}N_2O_3$	73.20 (73.31	5.51 5.59	7.62 7.77)
2,5-Diphenyl-3-(3-methylphenyl)-4-nitroisoxazolidine (**10b**)	91	90—92 (Ethanol)	$C_{22}H_{20}N_2O_3$	73.22 (73.31	5.48 5.59	7.64 7.77)
3-(4,4-Dimethylaminophenyl)-2,5-diphenyl-4-nitroisoxazolidine (**10c**)	78	103—105 (Benzene–hexane)	$C_{23}H_{23}N_3O_3$	70.88 (70.93	5.89 5.95	12.21 12.32)
3-(2-Methylphenyl)-2-phenyl-4-(phenylsulfonyl)isoxazolidine (**14a**)	89	112—114 (Ethanol–hexane)	$C_{22}H_{21}NSO_3$	69.55 (69.63	5.47 5.58	3.51 3.69)
3-(3-Methylphenyl)-2-phenyl-4-(phenylsulfonyl)isoxazolidine (**14b**)	82	87—89 (Ethanol–hexane)	$C_{22}H_{21}NSO_3$	69.58 (69.63	5.52 5.58	3.54 3.69)
6,6-Dimethyl-2,3,3a,4,5,6-hexahydro-5-phenyl-2-(phenylsulfonyl)pyrrolo-[1,2-*b*]isoxazole (**15**)	87	173—174 (Ethanol–hexane)	$C_{20}H_{23}NSO_3$	67.16 (67.21	6.39 6.48	3.80 3.92)



a) $R^1 = C(CH_3)_3$; $R^2 = H$; $R^3 = C(CH_3)_3$.
b) $R^1 = H$; $R^2 = C(CH_3)_3$; $R^3 = H$.

Fig. 1.

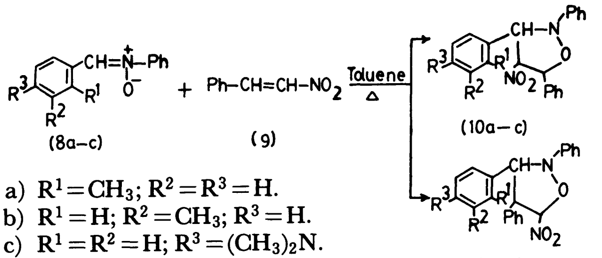
A new broad band in the visible spectrum, 475—498 nm, was observed immediately on mixing equimolar solutions of the fluoranil with each of the open chain nitrones (**8a,b,d,e**) in dichloromethatne (Table 1). These absorptions were ascribed to the charge-transfer complexes formation, since neither the fluoranil nor the nitrones (**8a,b,d,e**) alone absorb in this region (Table 1). However, the separation of the mixtures by preparative layer chromatography (PLC) did not give the corresponding amides even after prolonged heating, but the starting materials were recovered. Attempts to isolate these nitrone–fluoranil complexes in crystalline form were failed. These results may suggest that the charge-transfer interaction between the open chain nitrones and fluoranil are weak[9] to undergo rearrangement of **8a**—**c** to their corresponding amides.

On addition of the electron-deficient β-nitrostyrene (**9**) to each of the nitrones (**8a**—**c**) in dichloromethane at room temperature, pale yellow colored solutions were obtained, which gave no characteristic absorption band for charge-transfer complexes. This behavior can be ascribed to the relatively low electron affinity of the β-nitrostyrene.[9—11] After heating of the mixture of each of nitrones (**8a**—**c**) with β-nitrostyrene in toluene, only stable 4-nitroisoxazolidines (**10a**—**c**) were obtained, regiospecifically. This result is consistent with the

Table 3. Spectroscopic Data of Products Listed in Table 2

Compound	IR $\tilde{\nu}$/cm^{-1} (selected bands)	^{1}H-NMR δ	MS *m/z* (Rel intensity)
3a[7]	3120 (NH), 1711 (CO)	($CDCl_3$): 1.35 (9H, s, $C(CH_3)_3$), 1.40 (15H, s, $C(CH_3)_3$ and $C(CH_3)_2$), 7.15 (2H, dd, *J*=2Hz, phenyl protons), 8.6 (1H, s, NH)	273 (29, M^+), 258 (100), 230 (6)
3b[8]	3177 (NH), 1704 (CO)	($CDCl_3$): 1.31 (9H, s, $C(CH_3)_3$), 1.42(6H, s, $C(CH_3)_2$), 7.06 (3H, m, phenyl protons), 9.8 (1H, s, NH)	217 (60, M^+), 202 (100)
8d	1208 (NO), 1600 (C=N)	($CDCl_3$): 3.85 (6H, s, $2CH_3O$), 6.4—6.7 (1H, m, phenyl proton), 7.2—8.15 (2H, m, phenyl protons), 8.3 (1H, s, CH=N)	257 (50, M^+), 251 (5), 226 (100), 210 (8)
8e	1209 (NO), 1598 (C=N)	($CDCl_3$): 3.95 (3H, s, CH_3O), 3.97 (3H, s, CH_3O), 6.81 (1H, d, *J*=4Hz, phenyl proton), 7.1—7.81 (1H, m, phenyl proton), 7.82 (1H, s, CH=N), 8.85 (1H, d, *J*=1.5Hz, phenyl proton)	257 (5, M^+), 251 (50), 226 (100)
10a	1549 (NO_2)	(C_6D_6): 2.26 (3H, s, CH_3), 3.05 (1H, t, *J*=4Hz, H-4), 3.6 (1H, d, *J*=5Hz, H-3), 3.95 (1H, d, *J*=4Hz, H-5), 6.5—7.9 (14H, m, phenyl protons) ($CDCl_3$): 2.32 (3H, s, CH_3), 5.25 (1H, t, *J*=5Hz, H-4), 5.72 (2H, m, H-3 and H-5), 6.55—7.95 (14H, m, phenyl protons)	360 (42, M^+), 314 (10), 106 (26), 77 (100)
10b	1550 (NO_2)[a]	($CDCl_3$): 2.35 (3H, s, CH_3), 5.35 (1H, t, *J*=5Hz, H-4), 5.58 (1H, d, *J*=4Hz, H-3), 5.75 (1H, d, *J*=6Hz, H-5), 6.65—7.95 (14H, m, phenyl protons)	360 (26, M^+), 314 (9), 106 (22), 77 (100)
10c	1757 (NO_2)	($CDCl_3$): 2.28 (6H, s, $N(CH_3)_2$), 4.0 (1H, t, *J*=8Hz, H-4), 4.82 (1H, d, *J*=9Hz, H-3), 5.25 (1H, d, *J*=8Hz, H-5), 6.85—7.5 (14H, m, phenyl protons)	389 (5, M^+), 283 (10), 240 (10), 106 (20), 77 (100)
14a	1312, 1151 (SO_2)[a]	(C_6D_6): 2.35 (3H, s, CH_3), 3.85 (CH_2, dd, *J*=4 and 8Hz, H-5), 4.35 (1H, dd, *J*=4 and 8Hz, H-4), 5.35 (1H, d, *J*=4Hz, H-3), 6.24—8.05 (14H, m, phenyl protons)	379 (10, M^+), 363 (3), 141 (29), 77 (100)
14b	1305, 1145 (SO_2)	($CDCl_3$): 2.25 (3H, s, CH_3), 4.22 (CH_2, dd, *J*=4 and 7Hz, H-5), 4.41 (1H, dd, *J*=7 and 4Hz, H-4), 4.9 (1H, d, *J*=4Hz, H-3), 6.68—7.95 (14H, m, phenyl protons)	379 (12, M^+), 363 (5), 141 (32), 77 (100)
15	1308, 1142 (SO_2)	($CDCl_3$): 0.75 (3H, s, CH_3), 1.1 (3H, s, CH_3), 1.8—2.8 (3H, m, CH_2-3 and H-4), 3.05—3.6 (2H, m, H-4 and H-5), 3.75—4.45 (1H, m, H-3a), 5.25 (1H, dd, *J*=3 and 9Hz, H-2), 6.95—8.11 (10H, m, phenyl protons)	357 (6, M^+), 341 (2), 187 (29), 170 (17), 141 (35), 77 (100)

interaction between the frontier orbitals of the nitrones and the frontier orbitals of the electron-deficient dipolarophiles.[10,11] The observation of the methine proton signal of the 5-H at δ 5.25—5.75 for the cycloadducts (**10a—c**) respectively (Table 3) is indicative of the methine group being located between an oxygen atom and a nitro group.[10] Moreover, besides the molecular ions at *m/z* 360, 360, and 389 for the products (**10a—c**) respectively, an interesting fragment *m/z* 106 (20—26%), probably for the C_6H_5CHO structure (Table 3) was observed in their mass spectroscopic data. This is another strong evidence confirming the structure of the products, 4-nitroisoxazolidine isomers (**10a—c**).



a) $R^1=CH_3$; $R^2=R^3=H$.
b) $R^1=H$; $R^2=CH_3$; $R^3=H$.
c) $R^1=R^2=H$; $R^3=(CH_3)_2N$.
d) $R^1=OCH_3$; $R^2=H$; $R^3=OCH_3$.
e) $R^1=H$; $R^2=OCH_3$; $R^3=OCH_3$.

Fig. 2.

Treatment of the nitrones **8a,b**, and **12** with phenyl vinyl sulfone (**13**) did not form charge-transfer complexes, but instead they undergo 1,3-dipolar cycloaddition reactions giving the cycloadducts (**14a**, b), and (**15**). This behavior can also be attributed to the lower electron affinity of the phenyl vinyl

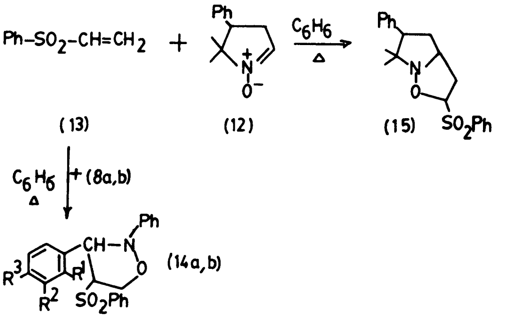


Fig. 3.

sulfone (0.8 eV) than that of fluoranil (0.97 eV).9,10)

While the reaction of the electron-deficient **13** with the nitrones (**8a,b**) afforded the 4-(phenylsulfonyl)-isoxazolidines (**14a,b**), a dipole highest occupied-dipolarophile lowest unoccupied controlled product, 5-(phenylsulfonyl)isoxazolidine (**15**), a dipole lowest unoccupied-dipolarophile highest occupied controlled product was obtained from the addition reaction of **13** to the nitrone **12**. The reversal of the regioselectivity in the case of the open chain nitrones may be ascribed to their high orbital energies, which favor of the 4-substituted isomers.10)

The distinction between the 4- and 5-(phenylsulfonyl)isoxazolidines (**14a,b**, and **15**, respectively), was provided by the chemical shift10) of the methylene protons. The signal for the CH_2 protons of the 4-(phenylsulfonyl)isoxazolidines (**14a,b**) appears at relatively low magnetic field δ 3.85 and 4.22, respectively, while the corresponding signal for the 5-(phenylsulfonyl)isoxazolidine (**15**) occurs at δ 1.18—2.80 (Table 3).

When each of the electron-deficient dipolarophiles (**9** and **13**) was added to the indole 1-oxides (**1a,b**) in dichloromethane (equimolar ratio), the solution turned pale yellow in color. Such solution gave no broad band for charge-transfer complexes. It is plausible to suggest that the results can be ascribed to the low electron affinity of the electron-deficient dipolarophiles (**9** and **13**). Heating of the solutions gave yellow unstable products, which could not be obtained in a pure form.

Experimental

All melting points are uncorrected. IR spectra were recorded (KBr) on a Perkin-Elmer 283 spectrophotometer. UV and visible spectra were measured with a Beckman spectrophotometer model 26. ^{1}H-NMR spectra were recorded on Varian EM-360 (60 MHz) NMR spectrometer using TMS as the standard. Mass spectra were obtained on a MAT 311A spectrometer operating at 70 eV. Elemental analysis were performed by the Microanalytical Unit of Cairo University. The nitrones **1a,b**,7,12) **8a—e**13), and **12**14) were prepared according to literature procedures.

Reaction of Nitrones (1a,b) with Tetrafluoro-2,5-cyclohexadiene-1,4-dione (2). General Procedure: To a solution of **1a** or **1b** (1 mmol) in 5 ml dry dichloromethane, 180 mg (1 mmol) fluoranil was added. The mixture was refluxed for 3 h and then the solvent was evaporated. The residue was chromatographed on a preparative layer chromatography (PLC) of silica gel, using a mixture of benzene-ethyl acetate (9:1) as eluent, to give one zone. Extraction with acetone and recrystallization from the appropriate solvent (Table 2) gave **3a** or **3b**.

Reaction of 5,5-Dimethyl-4-phenyl-Δ^1-pyrroline 1-Oxide (12) with 2. To a stirred solution of 100 mg (0.53 mmol) of **12** in 5 ml dry dichloromethane, 95 mg (0.53 mmol) of **2** in 2 ml of dichloromethane was added. The reaction mixture was refluxed for 12 h and then the solvent was evaporated. The residue was separated on PLC of silica gel, using a mixture of benzene-ethyl acetate (10:1) as eluent, to give two zones. Extraction with acetone and recrystallization from ethanol-hexane gave the starting materials **12** and **2**.

Charge-Transfer Complexes of Nitrones (8a,b,d,e) with 2. To a stirred solution of each of nitrones (**8a,b,d,e**) (0.5 mmol) in dry dichloromethane, 0.5 mmol of **2** in dichloromethane was added. A greenish-orange color appeared. The colored solution was refluxed for 12 h. The solvent was evaporated and the residue was chromatographed on PLC (benzene-ethyl acetate, (10:1). The starting materials, nitrones (**8a,b,d,e**) as well as fluoranil (**2**) were recovered.

Reaction of Nitrones (8a—c) with β-Nitrostyrene (9). Mixture of nitrone (**8a—c**) (1 mmol), β-nitrostyrene (**9**) (1 mmol) and dry toluene (10 ml) was heated to reflux for 12 h. The solvent was evaporated and the residue was separated on PLC (benzene). Extraction with acetone and recrystallization from the proper solvent (Table 2) afforded the products (**10a—c**).

Reaction of Nitrones (8a,b) and (12) with Phenyl Vinyl Sulfone (13). To a solution of each of nitrones (**8a,b**) and **12** (1 mmol) in 10 ml dry benzene, 168 mg (1 mmol) of phenyl vinyl sulfone was added. The reaction mixture was refluxed for 8 h and then the solvent was evaporated. The residue was separated on PLC (benzene) to give one zone. Extraction with acetone and recrystallization from a proper solvent gave the cycloadducts (**14a,b**, and **15**).

Reaction of Nitrones (1a,b) with 9. General Procedure: A solution of **1a** or **1b** (1 mmol) in 4 ml dichloromethane was added to a solution of **9** (1 mmol) in 4 ml dichloromethane. The resulting mixture was refluxed for 24 h. Evaporation of the solvent under reduced presure with rotary evaporator and chromatography of the residue on PLC of silica gel, using a mixture of benzene-ethyl acetate (10:1) as eluent, gave yellow unstable products, which could not be obtained in pure form.

Reaction of Nitrones (1a,b) with 13. Applying the same reaction conditons used for the reaction **1a,b** with **9**, the addition of **1a** or **1b** (1 mmol) to **13** (1 mmol) in dichloromethane gave also unstable products, which could not be identified.

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