

REACTION OF AZOMETHINE N-OXIDES. PART 4. A NEW MODE OF REACTION
OF AZOMETHINE N-OXIDES WITH DIBENZOYLACETYLENE

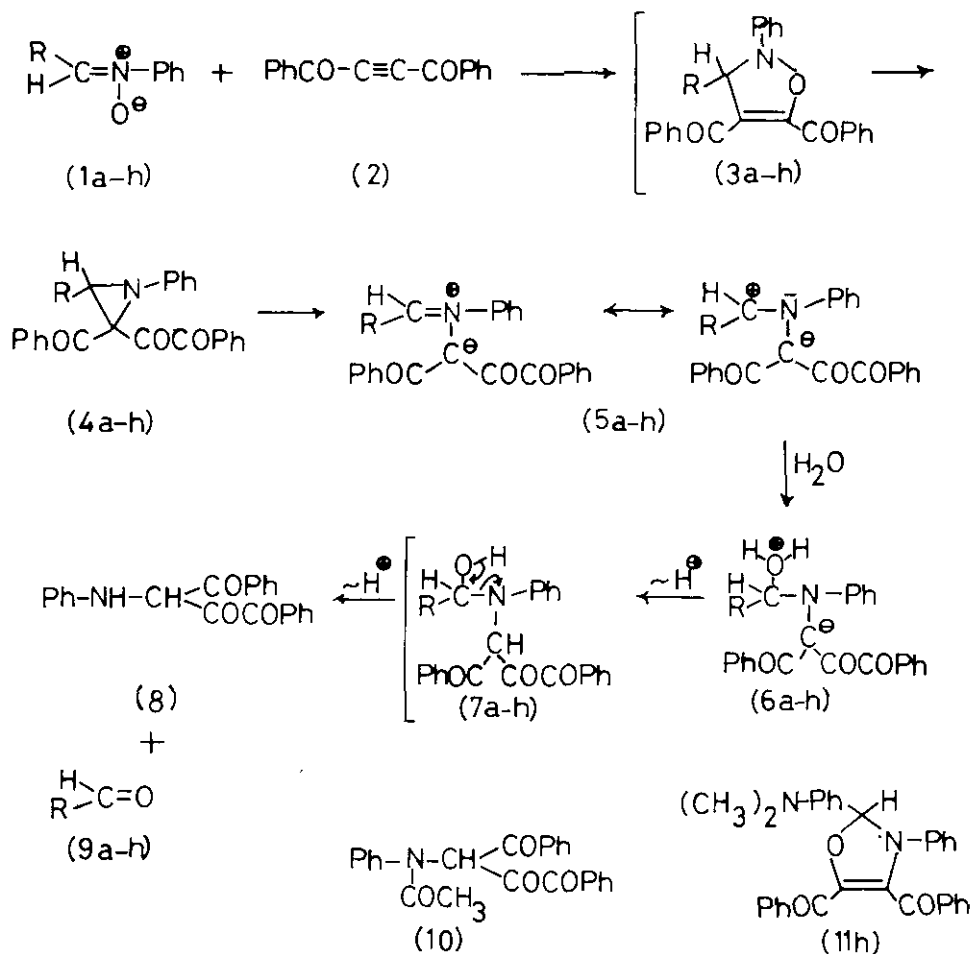
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Abstract - A new mode of 1,3-dipolar cycloaddition reaction with dibenzoylacetylene as dipolarophile was observed. The addition of this dipolarophile to different substituted open chain N-arylnitrones afforded 3-anilino-1,4-diphenylbutane-1,2,4-trione. Its formation by 1,3-dipolar cycloaddition reaction followed by intermolecular rearrangement and ylide decomposition is discussed. On the other hand, the conformationally rigid cyclic nitrones form either 4-oxazoline or enamine compounds.

Our interest in the reactions of azomethine N-oxides^{1,2} (nitrones) and azomethines³ with electron-deficient compounds leads us to investigate the cycloadditions of dibenzoylacetylene with nitrones. We recently reported that nitrones as well as azomethines form charge-transfer complexes with some electron-deficient compounds as tetracyanoethylene and 1,4-benzoquinones^{4,5}. We would now like to report the reaction of dibenzoylacetylene as an electron poor compound with various nitrones. The reactions of alkynes with nitrones are known to afford the thermally labile 4-isoxazoline^{6,7}, which can be isomerized via valence rearrangement to 2-acylaziridine^{8,9}. The formation of ylide as intermediate step has been postulated to explain the formation of the highly unstable 4-oxazoline¹⁰. In few cases, these ylides were isolated and identified^{6,11}. However, we found that the reactions of N-arylnitrones (1a-h) with dibenzoylacetylene (2), in methylene chloride at room temperature, yielded 3-anilino-1,4-diphenylbutane-1,2,4-trione (8) and the corresponding aldehyde^{12,13} (9a-h) (Scheme 1). Structure (8) (Scheme 1) was assigned to this product on the basis of analytical and spectroscopic data. The analytical data showed that the molecular formula is C₂₂H₁₇NO₃. The ir spectrum revealed absorption maxima for amino and carbonyl groups at 3450 and 1672 cm⁻¹, respectively. The formation of acetyl derivative (10) from the treatment of (8) with acetic anhydride and acetic acid also confirms the presence of the amino group in (8). The ¹H nmr spectrum of (8) gave the following signals: a broad singlet for both the methine and amino protons at 3.72 ppm as well as a multiplet for the phenyl protons at 6.5 - 8.25 ppm. Thus, both ir and nmr data confirm implicitly of the proposed structure of the trione (8).

However the structure (8) was evidently confirmed mass spectrometrically. Beside the molecular ion at m/e 343, two interested fragmentations at m/e 238 (15%) and 210 (40%) were observed, probably from the molecular ion by loss of the following radicals: $\text{Ph-C}^{\cdot}=\text{O}$ and Ph-CO-CO^{\cdot} , respectively. Moreover, the presence of a fragment at m/e 92 (17%), probably for the $\text{C}_6\text{H}_5^{\cdot}\text{NH}$ radical, further supports the structure 8.

All the results suggested that the thermally labile 4-isoxazoline (3a-h) formed isomerized via valence rearrangement to 2-acylaziridines (4a-h), which undergo ring opening to give ylides (5a-h). The addition of H_2O molecule (probably present in crystallisation solvents) to the ylides (5a-h) followed by hydrogen migration and carbon-nitrogen fission should lead to the formation of the trione (8) and the corresponding aldehydes (9a-h).



a; R=4- CH_3 - C_6H_4 . b; R=4- CH_3O - C_6H_4 . c; R=3,4-(CH_3O) $_2$ - C_6H_3 . d; R=3,4-methylenedioxyphenyl. e; R=4-Cl- C_6H_4 . f; R=4- NO_2 - C_6H_4 . g; R=2-thienyl. h; R=4-(CH_3) $_2$ N- C_6H_4 .

Scheme 1

As shown in Table 1, the yield of the trione (8) is high in the case of the nitrones which contain electron donating groups on the carbon of the nitrone functional group. This feature may be due to that the electron donating group should increase the stability of the ylide intermediate (5a-h) and consequently their life-time, which increases therefore the chance of the reaction of (8) with H_2O .

Table 1. Physical and analytical data of the reactions of the nitrones (1a-g) with dibenzoylacetylene

Reaction	Reaction time (h)	Yield of (8) (%)	Aldehyde		
			Compound	Mp°C ^a	Yield (%)
1a + 2	10	80	p-Tolualdehyde	112	12
1b + 2	8	76	p-Methoxybenzaldehyde	121 ^a	20
1c + 2	9	75	3,4-Dimethoxybenzaldehyde	121 ^a	19
1d + 2	12	47	3,4-Methylenedioxybenzaldehyde	37	23
1e + 2	15	44	p-Chlorobenzaldehyde	47	26
1f + 2	18	64	p-Nitrobenzaldehyde	106	17
1g + 2	14	36	2-Thiophenecarboxaldehyde	134 ^a	31

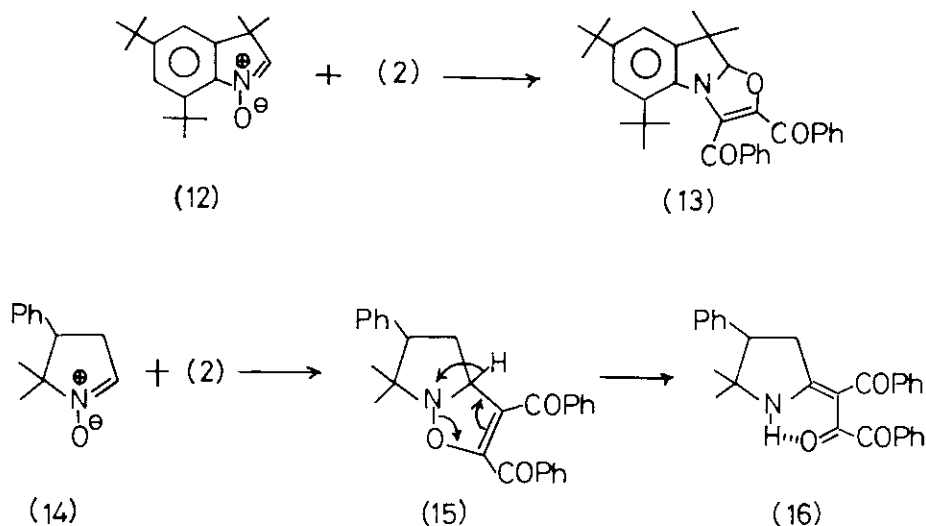
a Phenylhydrazone derivative

By contrast, the reaction of the dibenzoylacetylene with nitrone (1h), under the same conditions, afforded beside the trione (8) (32%) and the aldehyde¹² (9h) (9%), the thermally labile 4-oxazoline structure for the cycloadduct (11h) is based on the nmr data. The location of the methine proton signal at magnetic field as high as 6.58 ppm is indicative for the presence of the proton between nitrogen and oxygen atoms^{1,14}, and confirms the 4-oxazoline structure.

On the other hand, the reaction of the conformationally rigid nitrone (12) with the dipolarophile (2), in benzene at room temperature, gave only the 4-oxazoline (13) (Scheme 2); i.e. the trione (8) was not formed. The absence of any absorption in the amino and hydroxy groups region in ir spectrum is an evidence for the cyclic structure of (13). Also, the presence of the methine proton signal in the 6.9 - 7.9 ppm phenyl region in the ¹H nmr spectrum of (13) supports the suggested 4-oxazoline structure for (13).

As in the case of the reaction of the cyclic indole 1-oxide (12) with (2), the addition of the dipolarophile (2) to the cyclic pyrrole 1-oxide (14), in benzene at room temperature, did not give trione (8), but instead the rearrangement enamine (16). This structure (16) could be readily established on the basis of ir spectrum in KBr which revealed three bands at 3280, 1658 and 1605 cm^{-1} for an amino, conjugated carbonyl and carbon-carbon double bond groups, respectively.

As shown in the Scheme 2 the 1,3-dipolar cycloaddition reactions of the two conformationally



Scheme 2

rigid cyclic nitrones, indole 1-oxide (12) and pyrrole 1-oxide (14), have different reaction path. This behaviour means that the conformationally rigid structure of the two nitrones (12) and (14) seems to be responsible for this behaviour and the newly suggested rearrangement occurs only in the case of the open chain nitrones.

EXPERIMENTAL

Melting points, uncorrected, were determined on a Gallenkamp device. Infrared spectra were recorded on a Shimadzu-408 spectrometer using KBr disk. ¹H nmr spectra were determined on a Bruker WP 80 (80 MHz) and mass spectra were determined on a MAT 311A spectrometer operating at (70 eV). Elemental analyses were performed by the microanalytical unit at Cairo university. The nitrones (1a-h)¹⁵, (12)¹⁶ and (14)¹⁷ and dibenzoylacetylene¹⁸ were prepared according to the literature. A 1-mm layer of silica gel Merck PF₂₅₄ on a plates 20 cm by 48 cm was employed for preparative t.l.c. and bands were detected by exposure to short-wavelength ultraviolet light.

Reaction of nitrones (1a-g) with dibenzoylacetylene (2). General procedure.

To stirred solution of 1 mmol of nitron in 5 ml of methylene chloride 1 mmol of dibenzoylacetylene in 2 ml of methylene chloride was added. The stirring was continued at room temperature until the t.l.c. showed the disappearance of the starting compounds. The solvent was then removed at room temperature with rotary evaporator and the residue was crystallized from benzene-n-hexane to afford the 3-anilino-1,4-diphenylbutane-1,2,4-trione (8) as yellow crystals, mp 153-154 °C (Found: C, 76.81; H, 4.86; N, 3.94. C₂₂H₁₇NO₃ requires C, 76.95; H, 4.99; N, 4.08 %); ν_{max}. 3450 (NH), 1672 (C=O); m/e 343 (M, 4%), 342 (17%), 324 (3%), 238 (15%), 210 (40%), 105 (100%), 92 (17%); δ (CDCl₃)

3.72 (2H, broad, CH and NH), 6.5 - 8.25 (15H, m, ArH). The residue was chromatographed on a preparative t.l.c., using benzene as eluent to give three zones. Extraction of the major zone with acetone gave the corresponding aldehyde, which was identified by mp of the aldehyde or the phenylhydrazone derivative^{12,13}. The extraction of the other two zones gave small amounts of organic compounds, which could not be purified or identified.

3-(N-Acetyl-N-phenyl)-1,4-diphenyl-butane-1,2,4-trione (10)

To a solution of 100 mg (0.3 mmol) of (8) in 2 ml of acetic acid, 1 ml of acetic anhydride was added, then the solution was refluxed for 15 min. The mixture was poured in 5 ml of water. The solid which formed upon cooling was crystallized from ethanol, 70 mg (62 %) of (16), mp 168-170 °C, being obtained (Found: C, 74.65; H, 4.86; N, 3.57. $C_{24}H_{19}NO_4$ requires C, 74.79; H, 4.97; N, 3.63 %); ν_{max} 1768, 1727 and 1685 (C=O).

Reaction of nitron (1h) with dibenzoylacetylene (2)

234 mg (1 mmol) of (2) in 3 ml of methylene chloride was added to a solution of 240 mg (1 mmol) of nitron (1h) in 3 ml of methylene chloride. The mixture was stirred until the t.l.c. showed the disappearance of the starting compounds. The solvent was then removed at room temperature with rotary evaporator and the residue was then chromatographed on a thin-layer plate, using a mixture of benzene-ethyl acetate (10:2) as eluent, to give three zones. Extraction with acetone and crystallization of the first zone ($R_f=0.83$) afforded 120 mg (25%) 2-(4-N,N-dimethylaminophenyl)-4,5-dibenzoyl-3-phenyl- Δ^4 -oxazoline (11h) as colorless crystals, mp 183 - 184 °C (methylene chloride-n-hexane) (Found: C, 78.31; H, 5.47; N, 5.72. $C_{21}H_{26}N_2O_3$ requires C, 78.46; H, 5.52; N, 5.90 %); ν_{max} 1673 (C=O), 1625 (C=C); m/e 474 (M^+ , 20%), 369 (100%), 291 (27%), 105 (60%); δ (CDCl₃) 1.78 (3H, s, CH₃), 2.56 (3H, s, CH₃), 6.58 (1H, s, CH), 6.65-7.72 (19H, m, ArH).

Extraction of the second zone ($R_f=0.81$) with acetone and crystallization gave p-N,N-dimethylbenzaldehyde (9h), 14 mg (9%), mp 73-74 °C¹².

From the third zone ($R_f = 0.70$) 110 mg (32%) of (8) was obtained.

2,3-Dibenzoyl-5,7-di-tert-butyl-9,9-dimethyl-9,9a-dihydro[1,3]oxazolo[3,2-a]indole (13)

To a stirred solution of 200 mg (0.7 mmol) of 5,7-di-tert-butyl-3,3-dimethyl-3H-indole 1-oxide (10) in 3 ml of dry benzene, 162 mg (0.7 mmol) of dibenzoylacetylene in 5 ml of dry benzene was added. The stirring was continued for 6 h and then the solution was concentrated with rotary evaporator at room temperature. Upon cooling a pale yellow crystals, 80 mg (44%) of (12), mp 173-174 °C, were obtained, (Found: C, 80.31; H, 7.29; N, 2.58. $C_{34}H_{37}NO_3$ requires C, 80.44; H, 7.35; N, 2.76 %), ν_{max} 1661 (C=O); m/e 507 (M^+ , 5%), 402 (100%), 273 (70%), 105 (65%); δ (DMSO) 1.30 (3H, s, CH₃), 1.37 (9H, s, (CH₃)₃C), 1.58 (9H, s, (CH₃)₃C), 1.61 (3H, s, CH₃), 6.9-7.9 (13H, m, CH and ArH).

2-(5,5-Dimethyl-4-phenylpyrrolidin-2-ylidene)-1,4-diphenylbutane-1,2,4-trione (16)

A solution of 123 mg (0.53 mmol) of (2) in 3 ml of dry benzene was added to a stirred solution of 100 mg (0.53 mmol) of 5,5-dimethyl-4-phenyl- Δ^1 -pyrroline 1-oxide (13). The stirring was continued for 12 h and then the solvent was evaporated. The residue was chromatographed on a thin-layer plate, using a mixture of benzene-ethyl acetate (10:2) as eluent, to give two zones. Extraction of the first zone with acetone ($R_f = 0.57$) and crystallization gave 45 mg (20%) (16), as colorless crystals, mp 175-176 °C (ethanol-n-hexane) (Found: C, 79.28; H, 5.86; N, 3.19. $C_{28}H_{25}NO_3$ requires C, 79.41; H, 5.95; N, 3.31 %); ν_{max} : 3280 (NH), 1658 (C=O), 1605 (C=C); m/e 423 (M^+ , 9%), 405 (100%), 390 (10%), 318 (95%), 105 (96%); δ (CDCl₃) 0.95 (3H, s, CH₃), 1.52 (3H, s, CH₃), 3.5-3.9 (3H, m, CH₂ and CH), 7.0-8.0 (16H, m, ArH and NH).

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