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Reaction of Dimethylphenacylsulfonium Bromide with *N*-Nitrosoacetarylamides and Reactions of the Products with Nucleophiles[†]

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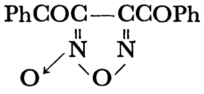
The azo coupling of dimethylphenacylsulfonium bromides (I) with *N*-nitrosoacetanilides in nonaqueous solvents, and with diazotized aniline in aqueous media gave 2-bromophenylglyoxal 2-arylhydrazones (V) and the tetrazine (VI), respectively. V reacted with nucleophiles displacing the bromide. Treatment of V with bases gave VI *via* benzoylphenylnitrilimine (X). 1,3-Dipolar cycloadditions of X onto ethyl acrylate and acrylonitrile afforded the expected cycloadducts. The mechanisms of the reactions are outlined.

Recently it has been reported that the nitrosation of dimethylphenacylsulfonium bromide (Ia) affords II[1)] or III[2)] depending on the reaction conditions. In view of the similarity between the azo coupling and nitrosation reaction, it was of interest to investigate the azo coupling of I in aqueous and nonaquous media to see whether or not similar effects would be observed. An earlier report[3)] claimed that coupling of benzenediazonium sulfate to Ia gives IV. The structure of the latter cannot be sustained, however. The azo coupling of I in nonaqueous media has not yet been explored. We now report the results of this reaction and some properties of the product formed.

$RC_6H_4COCH_2\overset{+}{S}(CH_3)_2Br^-$

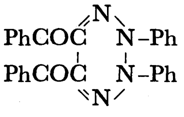
I



II

$PhCOC(Br){:}NOH$

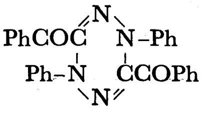
III



IV

$RC_6H_4COC(Br){:}NNHC_6H_4R'$

V

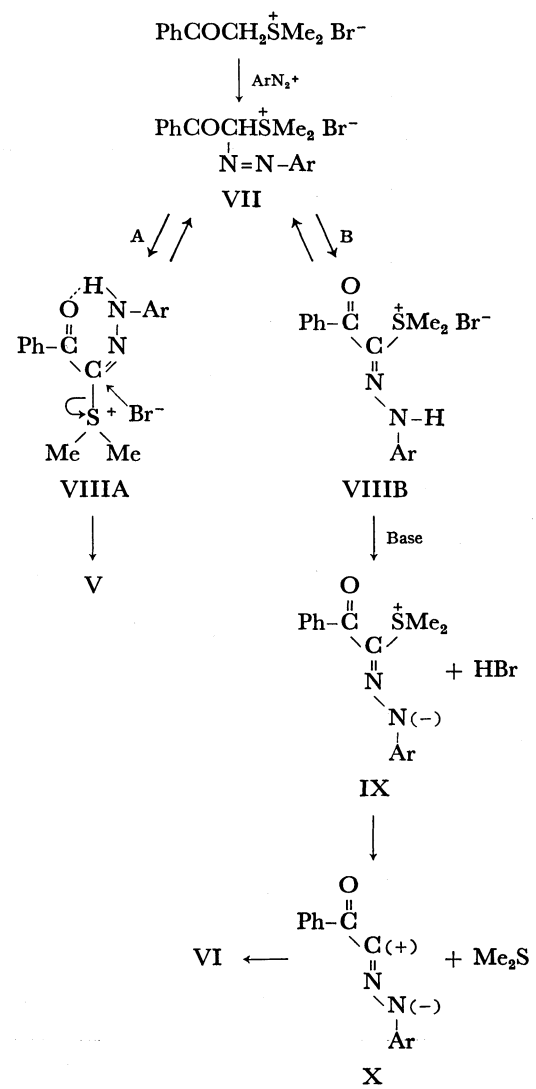


VI

a, R=H; b, R=4-Me; c, R=4-Br; d, $R=4\text{-}NO_2$

Results and Discussion

Treatment of Ia with *N*-nitrosoacetanilide in ether gave 2-bromophenylglyoxal 2-phenylhydrazone (Va, R=R′=H). The latter was also obtained when other organic solvents were used in place of ether. The structure of Va was established by elemental analysis, by molecular weight determination, and by analysis of its spectra (see Experimental). The reactions summarized in Scheme 2 also support structure Va for the reaction product. Similar treatments of Ib—d with *N*-nitrosoacetanilides in EtOH gave the products Vb—g (Table1).



A, in nonaqueous media; B, in aqueous media

Scheme 1.

Reaction of Ia with benzenediazonium chloride in NaOAc buffered solutions gave 1,4-diphenyl-3,6-dibenzoyl-1,4-dihydro-1,2,4,5-tetrazine (VI). The latter was identified by mixed melting point with an authentic sample[4)] and by spectral analysis. In addition, the formation of VI from Va upon treatment with bases

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[†] Taken in part from the Ph. D. Thesis of one of the authors (A. O. A).

TABLE 1. 2-BROMOPHENYLGLYOXAL 2-ARYLHYDRAZONES (V)
$RC_6H_4COC(Br){:}NNHC_6H_4R'$

Compound No.	R	R′	Mp[a] °C	Formula	Bromine, % Calcd	Bromine, % Found	λ_{max}^{EtOH} (log ε)
Va	H	H	114[c]	$C_{14}H_{11}BrN_2O$	26.36	26.11	372(4.169); 253(4.257)
Vb	H	4-Me	152	$C_{15}H_{13}BrN_2O$[b]	25.19	24.89	378(4.198); 253(4.258)
Vc	H	4-MeO	141	$C_{15}H_{13}BrN_2O_2$	23.98	24.10	386(4.223); 310(3.727); 253(4.329)
Vd	H	4-Cl	188	$C_{14}H_{10}ClBrN_2O$	23.67	23.48	372(4.205); 257(4.332); 229(4.333)
Ve	4-Me	H	125	$C_{15}H_{13}BrN_2O$	25.19	25.00	368(4.195); 257(4.214); 229(4.268)
Vf	4-Br	H	185	$C_{14}H_{10}Br_2N_2O$	41.83	41.78	374(4.178); 261(4.266); 227(4.296)
Vg	4-NO_2	H	188	$C_{14}H_{10}BrN_3O_3$	22.95	22.90	384(4.014); 320(3.908); 270(4.197) 229(4.364)

a) All compounds were crystallized from AcOH, except Va and Ve from EtOH. b) Anal. Calcd (Found): C, 56.80 (56.62); H, 4.13 (4.00); N, 8.83 (8.57)%. c) Lit., mp 113—114 °C.

TABLE 2. SUBSTITUTED 2-(PHENYLTHIO)PHENYLGLYOXAL 2-PHENYLHYDRAZONES (XI)

Compound No.	R	R′	Mp[a] °C	Formula	Sulfur, % Calcd	Sulfur, % Found	λ_{max}^{EtOH} (log ε)
$RC_6H_4COC(SC_6H_5){:}NNHC_6H_4R'$							
XIa	H	H	122	$C_{20}H_{16}N_2OS$[b]	9.64	9.41	370(4.278); 275(4.057); 243(4.306)
XIb	H	4-Me	137	$C_{21}H_{18}N_2OS$	9.26	9.31	376(4.258); 278(3.986); 245(4.275)
XIc	H	4-Cl	170	$C_{20}H_{15}ClN_2OS$	8.74	8.58	370(3.429); 290(3.304); 250(4.543)
XId	H	4-MeO	130	$C_{21}H_{18}N_2O_2S$	8.85	8.54	386(4.476); 310(3.945); 242(4.506)
XIe	4-Br	H	129	$C_{20}H_{15}BrN_2OS$	7.79	7.60	372(4.185); 270(4.171); 242(4.221)
$RC_6H_4COC(SC_6H_4Me\text{-}p){:}NNHC_6H_4R'$							
XIf	H	H	171	$C_{21}H_{18}N_2OS$[c]	9.26	9.30	368(4.443); 280(4.262); 242(4.522)
XIg	H	4-Me	126	$C_{22}H_{20}N_2OS$	8.89	8.79	378(4.335); 280(4.089); 244(4.390)
XIh	H	4-MeO	120	$C_{22}H_{20}N_2O_2S$	8.51	8.38	386(4.091); 285(3.811); 244(4.158)
XIi	H	4-Cl	145	$C_{21}H_{17}ClN_2OS$	8.42	8.51	374(4.306); 275(4.155); 245(4.348)
XIj	4-Br	H	132	$C_{21}H_{17}BrN_2OS$	7.54	7.32	374(4.189); 270(4.189); 245(4.246)

a) All compounds were recrystallized from EtOH. b) Anal. Calcd (Found): C, 72.25 (72.00); H, 4.85 (4.51); N, 8.42 (8.33)%. c) Anal. Calcd (Found): C, 72.80 (72.54); H, 5.23 (5.10); N, 8.08 (7.89)%.

TABLE 3. 2-(*p*-TOLYLSULFONYL)PHENYLGLYOXAL 2-ARYLHYDRAZONES (XII)
$RC_6H_4COC(SO_2C_6H_4Me\text{-}p){:}NNHC_6H_4R'$

Compound No.	R	R′	Mp[a] °C	Formula	Sulfur, % Calcd	Sulfur, % Found	λ_{max}^{EtOH} (log ε)
XIIa	H	H	174	$C_{21}H_{18}N_2O_3S$[b]	8.47	8.24	352(4.262); 270(4.123); 249(4.229)
XIIb	H	4-Me	184	$C_{22}H_{20}N_2O_3S$	8.17	8.08	374(4.357); 273(4.163); 253(4.326)
XIIc	H	4-Cl	180	$C_{21}H_{17}N_2O_3SCl$	7.76	7.81	365(4.360); 272(4.218); 247(4.355)
XIId	H	4-MeO	154	$C_{22}H_{20}N_2O_4S$	7.85	7.70	390(4.399); 255(4.366); 229(4.399)
XIIe	4-Me	H	178	$C_{22}H_{20}N_2O_3S$	8.17	8.00	364(4.308); 275(4.201); 230(4.364)
XIIf	4-Br	H	158	$C_{21}H_{17}BrN_2O_3S$	7.01	6.96	369(4.301); 275(4.267); 255(4.274) 231(4.356)
XIIg	4-NO_2	H	200	$C_{21}H_{17}N_3O_5S$	7.57	7.39	370(4.156); 270(4.190); 255(4.210) 235(4.197)

a) All compounds were crystallized from AcOH. b) Anal. Calcd (Found): C, 66.64 (66.38); H, 4.79 (4.59); N, 7.41 (7.52)%.

supports its structure. These results indicate that the diazonium coupling product of Ia in aqueous media is VI, and not IV as proposed[3] previously.

The probable mechanism that accounts for the foregoing results is presented in Scheme 1. It is assumed that the configurations of the hydrazone intermediate VIII in the solvents determined the products obtained.[1]

A brief chemical study of the product V is summarized in Scheme 2. The results show that V is highly reactive and reacts with nucleophiles with displacement of its halogen atom, and with bases to form the 1,3-dipolar intermediate X, that readily undergoes dimerization and 1,3-dipolar cycloaddition reactions. The structures of the products XI—XV follow from their method of preparation, the physical data, and their independent syntheses. The orientation of the cycloadditions of X

TABLE 4. SUBSTITUTED 2-CYANOPHENYLGLYOXAL 2-PHENYLHYDRAZONES (XIII)
$RC_6H_4COC(CN){:}NNHC_6H_4R'$

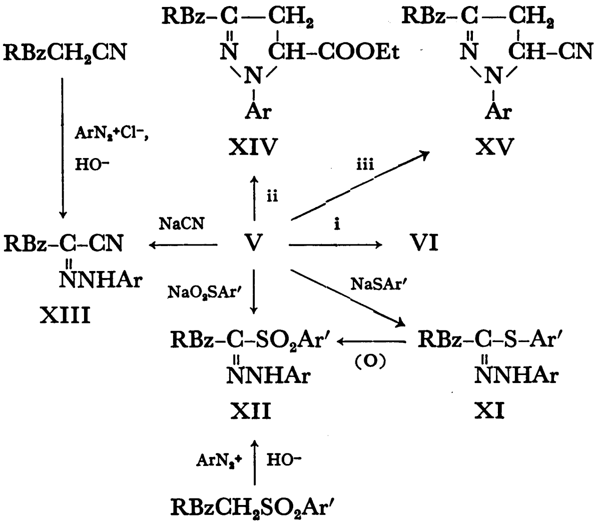
Compound No.	R	R′	Mp[a] °C	Formula	Nitrogen, % Calcd	Nitrogen, % Found	λ_{max}^{EtOH} (log ε)
XIIIa	H	H	135	$C_{15}H_{11}N_3O$	16.86	16.71	373(3.732); 280(3.605); 248(3.893)
XIIIb	H	4-Me	154	$C_{16}H_{13}N_3O$	15.96	16.01	384(4.301); 280(3.801)sh; 250(4.037)
XIIIc	H	4-Cl	174	$C_{15}H_{10}ClN_3O$	14.81	14.64	378(4.390); 280(3.869); 298(4.153)
XIIId	H	4-MeO	146	$C_{16}H_{13}N_3O_2$	15.04	14.88	400(4.185); 290(3.693)[b]; 250(3.914)
XIIIe	4-Me	H	149	$C_{16}H_{13}N_3O$	15.96	16.00	374(4.356); 285(3.909); 247(4.131)
XIIIf	4-Br	H	181	$C_{15}H_{10}BrN_3O$	12.80	12.63	370(4.375); 280(4.165); 245(4.376)
XIIIg	4-NO_2	H	233	$C_{15}H_{10}N_4O_3$	19.04	18.89	376(4.467); 265(4.200)

a) All compounds were recrystallized from EtOH. b) Broad band.

TABLE 5.

Compound No.	R	R′	Mp[a] °C	Formula	Nitrogen, % Calcd	Nitrogen, % Found	λ_{max}^{EtOH} (log ε)
1-Aryl-3-aroyl-5-ethoxycarbonyl-2-pyrazolines (XIV)							
XIVa	H	H	105	$C_{19}H_{18}N_2O_3$[b]	8.69	8.60	390(4.374); 254(4.244)
XIVb	H	4-Me	125	$C_{20}H_{20}N_2O_3$	8.33	8.07	400(4.299); 256(4.187)
XIVc	H	4-Cl	126	$C_{19}H_{17}ClN_2O_3$	7.85	7.69	390(4.330); 310sh(3.518); 260(4.179)
XIVd	4-Me	H	92	$C_{20}H_{20}N_2O_3$	8.33	8.11	392(4.375); 290sh(4.003); 253(4.189)
XIVe	4-Br	H	107	$C_{19}H_{17}BrN_2O_3$	6.98	6.69	398(4.283); 275sh(4.084); 260(4.126)
1-Aryl-3-aroyl-5-cyano-2-pyrazolines (XV)							
XVa	H	H	139	$C_{17}H_{13}N_3O$[c]	15.26	15.09	376(4.214); 240(4.142)
XVb	H	4-Me	118	$C_{18}H_{15}N_3O$	14.52	14.31	386(4.196); 248(4.134)
XVc	H	4-Cl	135	$C_{17}H_{12}ClN_3O$	13.56	13.48	374(4.442); 254(4.448)
XVd	H	4-MeO	135	$C_{18}H_{15}N_3O_2$	13.76	13.59	396(4.214); 244(4.181)
XVe	4-Br	H	165	$C_{17}H_{12}BrN_3O$	11.86	11.70	380(4.200); 270(4.200)

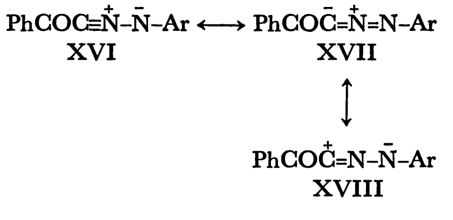
a) All compounds were recrystallized from EtOH. b) Anal. Calcd (Found): C, 70.79 (70.54); H, 5.63 (5.48)%.
c) Anal. Calcd (Found): C, 74.17 (73.88); H, 4.76 (4.54)%.



Reagents: i, Et_3N, NaOH, NaOPh, or NaOAc;
ii, $CH_2{=}CHCOOEt$; iii, $CH_2{=}CHCN$
$RBz = RC_6H_4CO$; $Ar = R'C_6H_4$;
$Ar' = C_6H_5$ or *p*-MeC_6H_4

Scheme 2.

can be interpreted in a manner similar to that proposed for benzoyl cyanide *N*-oxide;[11] *i.e.*, the resonance structures of X would be XVI, XVII, and XVIII, and its principal polarized structure would be XVIII:



$$PhCOC{\equiv}\overset{+}{N}{-}\overset{-}{N}{-}Ar \longleftrightarrow PhCO\overset{-}{C}{=}\overset{+}{N}{=}N{-}Ar$$

XVI XVII

$$\updownarrow$$

$$PhCO\overset{+}{C}{=}N{-}\overset{-}{N}{-}Ar$$

XVIII

Experimental

Mp's are uncorrected. IR and UV spectra were recorded on Unicam SP1000 and Unicam SP8000 spectrophotometers respectively. NMR spectra were recorded on Varian T60-A spectrometer with TMS as an internal standard. Microanalyses were carried out by Alfred Bernhardt, Mikroanalytisches Laboratorium, West Germany.

Reaction of I with N-*Nitrosoacetanilides.* A mixture of Ia[9] (0.1 mol) and *N*-nitrosoacetanilide[10] (0.12 mol) was stirred in ether for 8 hr at room temperature. Removal of the solvent gave Va (62%), mp 114 °C (EtOH); spectral characteristics: ν_{max} (KBr) 1650 (PhCO), 3240 (NH) cm^{-1}; λ_{max}^{EtOH} (log ε) 372 (4.169), 253 (4.257) nm; δ ($CDCl_3$) 7.5—6.5 (m, 10, ArH), 8.05 (s, 1, NH) ppm. The product Va was also obtained (55—80%) when the reaction was repeated using dioxane, chloroform, acetone, or EtOH in place of ether. The products Vb—g (Table 1) were similarly prepared using EtOH as a solvent.

Reaction of Ia with Benzenediazonium Chloride. To Ia (0.02 mol) in 50 ml EtOH was added NaOAc (8 g, in 30 ml water). The mixture was chilled (0—5 °C), vigorously stirred, treated dropwise (25 min) with PhN$_2$Cl (0.021 mol), and kept in an ice chest (3 hr). The solid was collected, washed with water, and recrystallized from EtOH to give VI (67%), mp and mixed mp[4] 198 °C; $\lambda_{\max}^{\mathrm{EtOH}}$ (log ε): 390 (2.749), 290sh (4.412), 265 (4.542); IR $\nu_{\max}$ (KBr) 1670 (PhCO) cm^{-1}, NH band was absent; its NMR spectrum (CDCl$_3$) showed only an aromatic proton multiplet.

Reaction of Va with Bases. A mixture of Va (0.01 mol) in EtOH (30 ml) and NaOAc (1 g) in water (5 ml) was refluxed for 30 min and cooled. Working up the reaction mixture gave VI (70%); mp and mixed mp with the sample above 198 °C. VI was similarly obtained by using one equivalent of NaOH or two equivalents of Et$_3$N in place of NaOAc.

Reactions of V with Nucleophiles, General. Equimolecular quantities of V and the appropriate nucleophile (NaSAr, NaO$_2$SAr, or NaCN) in EtOH were stirred for 0.5—2 hr and left overnight at room temperature. The product was collected, washed with water and recrystallized from EtOH or AcOH. The compounds XI—XIII prepared are listed in Tables 2—4. The products XIIh and XIIIa proved to be identical with authentic samples.[6,7] Reaction of Va with NaOPh, when carried out in a similar manner, gave VI (68%). IR (KBr) of XII showed bands at 1314 and 1140 cm^{-1} due to -SO$_2$- asymmetric and symmetric stretchings, and that of XIII exhibited a nitrile band at 2225 cm^{-1}. Both XII and XIII showed common bands at 1650 (PhCO) and 3260—3220 (hydrazone NH) cm^{-1}. UV spectral characteristics of XI—XIII are given in Tables 2—4.

Oxidation of XI. To a solution of XI (2 mmol) in AcOH was added 2 ml of hydrogen peroxide solution (33%); the mixture was left for two days at room temperature, then poured on water. Recrystallization of the product from AcOH gave the corresponding XII (73—78%). Mixed mp with samples prepared above showed no depression.

Formation of XIV and XV, General. A stirred cold solution of equimolecular quantities (5 mmol each) of V and ethyl acrylate (or acrylonitrile) in dry benzene (50 ml) was treated dropwise (30 min) with triethylamine (0.4 ml) in 10 ml of benzene. The mixture was then refluxed for 30 min and left overnight at room temperature, and filtered. The oil residue left after removal of the solvent solidified on trituration with petroleum ether (60/80 °C). Recrystallization from EtOH gave XIV (and XV) (Table 5) in 50—60% yields. The spectral characteristics of XIVa and XVb, taken as typical examples of the series prepared, are as follows: XIVa: $\nu_{\max}$ (KBr) 1650 (3-PhCO), 1755 (5-EtOCO) cm^{-1}; δ (CDCl$_3$) 7.0—8.5 (m, 10, ArH), 4.95 (t, 1, J=10 Hz, 5-CH), 3.65 (d, 2, J=10 Hz, 4-CH$_2$), 4.25 (q, 2, J=7 Hz, -COO$\underline{\mathrm{CH}}_2$-CH$_3$), 1.25 (t, 3, J=7 Hz, -COOCH$_2$-$\underline{\mathrm{CH}}_3$) ppm. XVa: $\nu_{\max}$ (KBr) 1650 (PhCO) cm^{-1}; δ (CDCl$_3$) 7.1—8.5 (m, 10, ArH), 3.77 (d, 2, J=10.5 Hz, 4-CH$_2$), 5.12 (t, 1, J=10.5 Hz, 5-CH) ppm. The UV maxima of XIV and XV are given in Table 5. The absence of nitrile absorption in the IR spectrum of XVa supports its 5-cyano structure.[8]

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