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N-[(N-Nitrosoarylamino)methyl]succinimide as a New Agent Generating Aromatic Diazotate

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We have newly synthesized a series of N-[(N-nitrosoarylamino)methyl]succinimides, disclosing their *syn* and *anti* equilibria in a state of solution. It has been found that these nitrosoamines are capable of furnishing aromatic diazotates in basic media. By allowing the generating aromatic diazotates to react *in situ*, azo-couplings and triazene formations have been provided. The nitrosoamines behaved in acidic media to suffer a migration of the nitroso group similarly to the Fischer-Hepp migration.

Keywords——N-[(N-nitrosoarylamino)methyl]succinimide; new reagent; aromatic diazotate; N-nitroso compound in basic medium; N-nitroso compound in acidic medium; isomers of N-nitroso compound; azo-coupling; triazene; nucleophilic substitution; migration of nitroso group

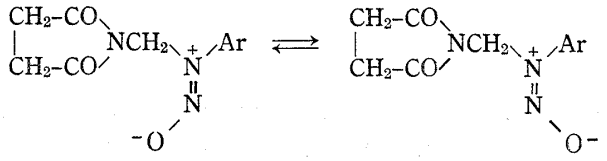
In continuation of the earlier work[2] on developing a new method for synthesizing diazoalkanes from N-[(N-nitrosoalkylamino)methyl]amides, we now wish to report reactions of their aryl analogs, N-[(N-nitrosoarylamino)methyl]succinimides (I) as new agents generating aromatic diazotates. These nitroso compounds were found to produce aromatic diazotates in a basic medium and to suffer migration of the nitroso group in acidic medium, similarly to that of the Fischer-Hepp migration.[3]

In the present paper we describe conformational analysis of *syn* and *anti* isomers of these new types of nitroso compounds and reactions of these compounds in basic media involving diazotate intermediate *in situ* and that in acidic media involving migration of the nitroso group.

Conformational Analysis of I

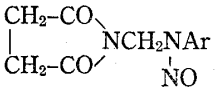
A variety of N-(arylaminomethyl)succinimides, prepared[4] from succinimide, formaldehyde and the corresponding aromatic primary amines, were easily nitrosated in the usual way. New eleven N-nitroso derivatives are listed in Table I with their physical and analytical data. As indicated in Table II nuclear magnetic resonance (NMR) spectra of these indicated the presence of equilibrium mixtures of the *syn* and *anti* isomers in deuteriochloroform, exhibiting two sets of signals, intensities of which were maintained constant even after immediate measurement. According to the previously reported[2] information about the isomers of N-[(N-nitrosoalkylamino)methyl]amides, it should be possible to assign the *syn* and *anti* isomers from the fact that the central methylene protons of the *cis* isomer with respect to the nitroso-oxygen resonate at a higher magnetic field that those of the *trans* isomer. Therefore, the *syn* and *anti* equilibrium ratio in deuteriochloroform can be given by the intensity ratio of the singlets at *ca.* δ 5.5 and at *ca.* δ 6.1.

1) Location: *Oshika, 2-2-1, Shizuoka-shi, 422, Japan.*
2) M. Sekiya, Y. Ohashi, Y. Terao, and K. Ito, *Chem. Pharm. Bull.* (Tokyo), **24**, 369 (1976).
3) O. Fischer and E. Hepp, *Ber.*, **19**, 2991 (1886); for a review, see S.R. Sandler and W. Karo, "Organic Functional Group Preparations," Vol. 2, Academic Press, Inc., New York, 1971, pp. 383—395.
4) M.B. Winstead, K.V. Anthony, L.L. Thomas, R.G. Strachan, and H.J. Richwine, *J. Chem. Eng. Data*, **7**, 414 (1962) [*C.A.*, **58**, 6722 (1963)]; M. Sekiya and K. Ito, *Chem. Pharm. Bull.* (Tokyo), **15**, 1339 (1967); M.E. Masanguy, A.J.A. Guevauviller, and D.F. Coignard, Fr. Patent M4175 (1966) [*C.A.*, **68**, 59139 (1968)].



I *syn* *anti*

TABLE I. N-[(N-Nitrosoarylamino)methyl]succinimides (I)



Compound No.	Ar	Appearance (Recryst. solvent)	mp (°C)	UV λ_{max}^{EtOH} nm[a] (log ε)	Formula	Analysis (%) Found (Calcd.) C	H	N
Ia	C_6H_5	prisms ($(CH_3)_2CO$)	140—141	264.5 (3.73)	$C_{11}H_{11}O_3N_3$	56.71 (56.65)	4.69 (4.75)	17.91 (18.02)
Ib	*m*-$CH_3C_6H_4$	needles (AcOEt)	71— 73	268.0 (3.64)	$C_{12}H_{13}O_3N_3$	58.34 (58.29)	5.35 (5.30)	16.96 (17.00)
Ic	*p*-$CH_3C_6H_4$	needles ($(CH_3)_2CO$)	138—140	270.0 (3.74)	$C_{12}H_{13}O_3N_3$	58.34 (58.29)	5.34 (5.30)	17.11 (17.00)
Id	*p*-$CH_3OC_6H_4$	prisms ($(CH_3)_2CO$)	125—126	224.5 280.5 (4.27) (3.88)	$C_{12}H_{13}O_4N_3$	54.46 (54.75)	5.10 (4.98)	15.60 (15.96)
Ie	*p*-$(CH_3)_2NC_6H_4$	needles ($(CH_3)_2CO$)	142 (decomp.)	257.0 310.5 (4.95) (3.92)	$C_{13}H_{16}O_3N_4$	56.49 (56.51)	5.85 (5.84)	20.38 (20.84)
If	3-C_5H_4N	needles (MeOH)	137—138	270.0 (3.80)	$C_{19}H_{10}O_3N_4$	50.81 (51.28)	4.23 (4.30)	23.68 (23.92)
Ig	2-C_5H_4N	needles (MeOH)	125—126	276.0 (3.88)	$C_{10}H_{10}O_3N_4$	51.17 (51.28)	4.39 (4.30)	24.07 (23.92)
Ih	*o*-$CH_3C_6H_4$	prisms (AcOEt)	103—105	250.0(sh) (3.78)	$C_{12}H_{13}O_3N_3$	58.37 (58.29)	5.32 (5.30)	17.13 (17.00)
Ii	*o,o'*-$(CH_3)_2C_6H_3$	prisms (EtOH)	137—139	250.0(sh) (3.64)	$C_{13}H_{15}O_3N_3$	59.89 (59.76)	5.84 (5.79)	16.18 (16.08)
Ij	*o*-$C_2H_5C_6H_4$	prisms ($(C_2H_5)_2O$)	74— 75	246.5(sh) (3.68)	$C_{13}H_{15}O_3N_3$	59.74 (59.76)	5.77 (5.79)	15.98 (16.08)
Ik	*o*-$CH_3OC_6H_4$	prisms (EtOH)	149—150	275.0 (3.56)	$C_{12}H_{13}O_4N_3$	54.77 (54.75)	4.99 (4.98)	16.03 (15.96)

a) sh: shoulder

TABLE II. NMR Spectral Data[a] of I

Compound No.	Ratio (%) *syn*	Ratio (%) *anti*	δ-Values (ppm) N-CH_2-N *syn*	N-CH_2-N *anti*	CH_2-CO, N, CH_2-CO *syn*	CH_2-CO, N, CH_2-CO *anti*
Ia	76	24	5.55	6.10	2.57	2.66
Ib	77	23	5.52	6.08	2.59	2.67
Ic	72	28	5.50	6.07	2.55	2.67
Id	67	33	5.49	6.05	2.56	2.66
Ie	67	33	5.44	6.03	2.53	2.63
If	72	28	5.65	6.24	2.65	2.72
Ig	100	0	5.80		2.59	
Ih	38	62	5.50	6.08	2.50	2.65
Ii	16	84	5.42	5.96	2.50	2.61
Ij	40	60	5.49	6.05[b] 6.15	2.53	2.68
Ik	45	55	5.50	6.05	2.51	2.61

a) measured in 10% $CDCl_3$ solution
b) The two hydrogens of this methylene exhibited two doublets owing to non-equivalence.

Bulkier alkyls of N-[(N-nitrosoalkylamino)methyl]amides were reported to be favorable for producing *syn* isomers. It was, however, observed that, in the nitroso compounds (Ih—k) possessing the *ortho*-substituted phenyl as an aryl, the *anti* isomers were predominant over *syn* isomers as can be seen in Table II. Steric inhibition of the mesomerism in these nitroso compounds is indicated by the ultraviolet (UV) spectral data shown in Table I and representatively in Fig. 1. The shift of the absorption maximum at 264.5 nm of N-[(N-nitrosoanilino)methyl]succinimide (Ia) to a shorter wavelengh was observed when the *ortho*-substituents are present on the benzene rings. Deviations from the coplanarity in the ph–$\overset{|}{N}^{+}$=N–O^{-} grouping by the introduction of the *ortho*-substituents would allow the favorable conformation shown in Fig. 2.

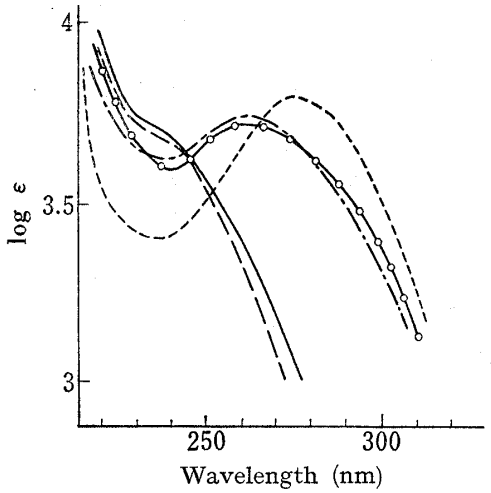


Fig. 1. UV Spectra of I in EtOH

—○—: Ia ——: Ih ------: Ii
——: If ·····: Ig

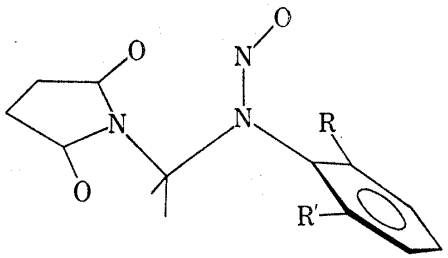


Fig. 2

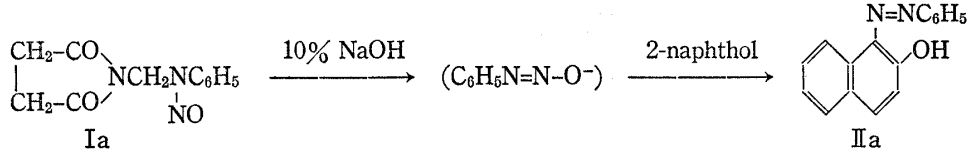
In this non-planar conformation the *anti* conformation appeared to be favorable to receive smaller repulsion of the nitroso-oxygen by the benzene ring than by the succinimide system.

In the case of the *o*-ethyl substituent the non-equivalence of the methylene protons as indicated by the two doublet signals (see Table II) is presumably due to closer approach of the bulkier *o*-ethyl to the methylene in the *anti* conformation.

In the case of N-[(N-nitroso-2-pyridylamino)methyl]succinimide (Ig) its equilibrium lies almost to the *syn* isomer. When compared with the 3-pyridyl derivative this observation appears to be due to the stronger mesomeric interaction in the 2-pyridyl derivative.

Reactions of I

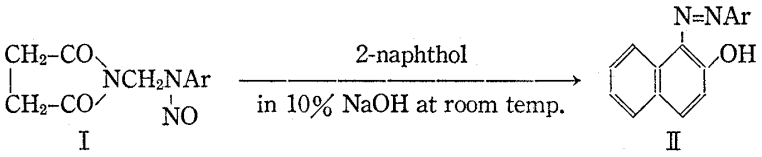
Easy alkali decomposition of Ia into phenyl diazotate was shown to occur from the azo-coupling reaction of 2-naphthol with this nitroso compound in alkaline medium. This reaction proceeded smoothly at room temperature to give 1-phenylazo-2-naphthol (IIa) in 85% yield when the nitroso compound was added to a solution in 10% aqueous sodium hydroxide.



Based on this fact, we succeeded in developing a use of a variety of N-[(N-nitrosoarylamino) methyl]succinimides (I) as new diazotate-generating agents. In the same manner as described above, the azo-coupling of 2-naphthol sufficiently proceeded with the nitroso com-

pounds possessing varied aryl groups, as summarized in Table III. In addition, the coupling reaction was extended to that of a number of active methylene compounds as shown in Table IV. The azo-coupling products including two new compounds were assigned as the corresponding phenylhydrazones from their analytical and spectral data.

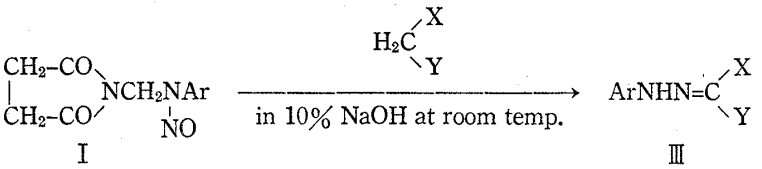
Table III. Azo-coupling of 2-Naphthol



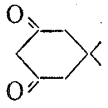
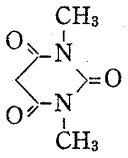
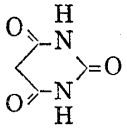
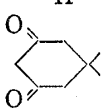
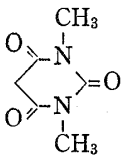
I II

Ar	React. period (hr)	Product No.	Yield (%)
C_6H_5	2	IIa	85
p-$CH_3C_6H_4$	2	IIb	92
p-$CH_3OC_6H_4$	2	IIc	97
p-$(CH_3)_2NC_6H_4$	3	IId	89
o-$CH_3C_6H_4$	2	IIe	87
3-C_5H_4N	1.5	IIf	56

Table IV. Azo-coupling of Active Methylene Compounds

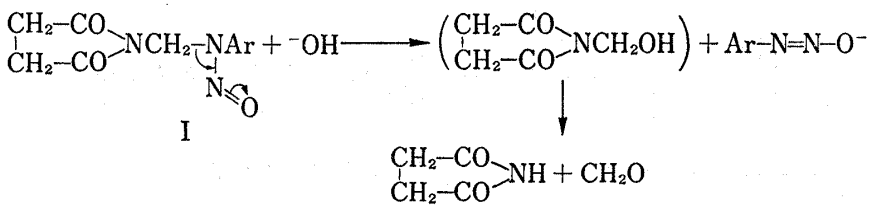


I III

Ar	H_2C (X, Y)	React. period (hr)	Product No.	Yield (%)
C_6H_5		5	IIIa	78
C_6H_5		5	IIIb	85
C_6H_5		4	IIIc	82
3-C_5H_4N		7	IIId	57
3-C_5H_4N		5	IIIe	61

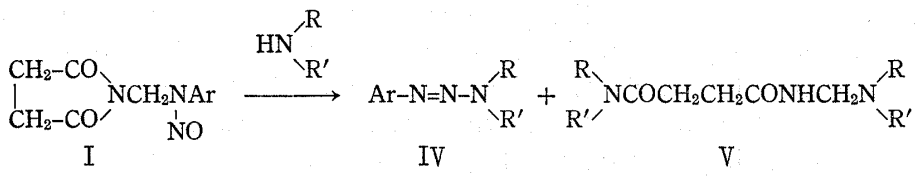
The formation of an aromatic diazotate from the nitroso compound seems mechanistically comparable with the previously reported diazoalkane formation from N-[(N-nitrosoalkylamino)methyl]amide.[2] In the latter reaction of the compound possessing a secondary

amide the substitution through β-elimination has been reported, whereas in the former compound of such imide type the β-elimination path is excluded and a direct nucleophilic substitution may be plausible.



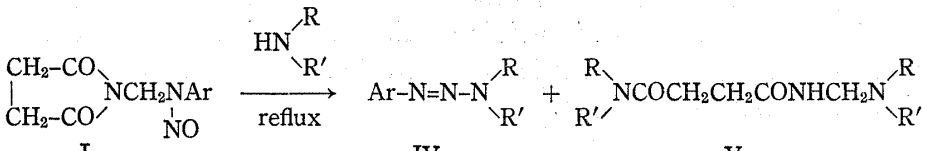
When the nitroso compound (Ia) was allowed to react with methanolic methoxide on heating at 40—45°, biphenyl was obtained in 50% yield. Taking account of evolution of nitrogen during the reaction, the formation of biphenyl indicates an occurrence of the coupling through decomposition of the diazotate.

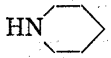
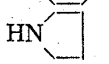
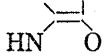
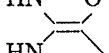
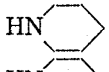
The function of aliphatic secondary amines in the reaction with nitroso compound was notable. On heating the nitroso compound in secondary amine at a refluxing temperature the reaction proceeded to give triazene (IV) and γ- dialkylamino-N-(dialkylaminomethyl)-γ-oxobutyramide (V). Results are shown in Table V.



The successful synthesis of 1-(2-pyridylazo)piperidine (IVe) shows that difficulty in synthesizing this compound through the usual diazotization of 2-aminopyridine is overcome by the present method.

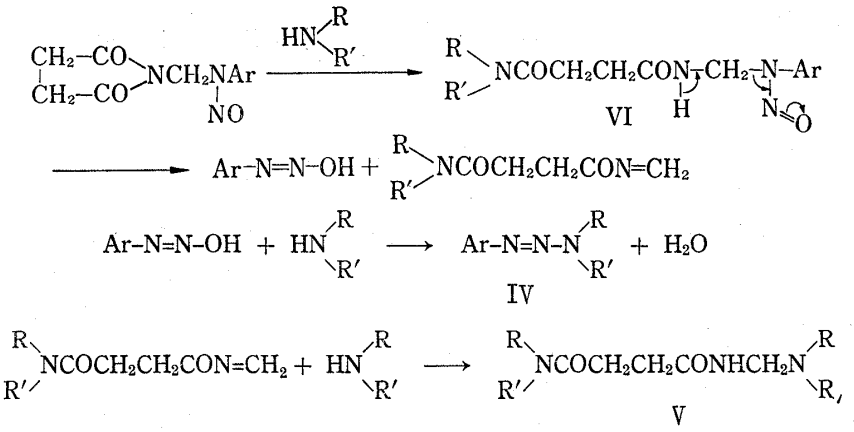
Table V. Reaction with Secondary Amines



Ar	HN(R)R′	React. period (hr)	Triazene No.	Yield (%)
C_6H_5		2	IVa	82
C_6H_5		1.5	IVb	77
C_6H_5		9	IVc	72
p-$CH_3C_6H_4$		2	IVd	79
2-C_5H_4N		1.5	IVe	60
3-C_5H_4N		1.5	IVf	64

In this reaction precedence of ring-opening of the succinimide residue was disclosed by the fact that, when the reaction of Ia with morpholine was stopped in an early stage, most of the nitroso compound was converted into 1-morpholino-N-[(N-nitrosoanilino)methyl]-γ-

oxobutyramide. The reaction giving triazene (IV) and V is, therefore, considered to proceed *via* γ-dialkylamino-N-[(N-nitrosoarylamino)methyl]-γ-oxobutyramide (VI) probably through the β-elimination path, as shown in the following.



The above results seem to provide evidence for usefulness of the nitroso compounds as new diazotate-generating agents. The nitroso compounds are stable enough to be stored indefinitly, in contrast to N-nitroso-N-acylamines[5]as the known diazotate-generating agent which decomposes on storage, sometimes explosively. It is possible to generate, *in situ*, diazotates such as 2-pyridyl derivative, which is not easily feasible by the conventional diazotization of aromatic amines. The method is, however, rather suitable for generation of the diazotates possessing electron-donating substituents on the phenyls, since synthesis of N-(arylaminomethyl)succinimide possessing such aryls is easier than that possessing electron-withdrawing substituents.

Examination was then made on chemical properties of the nitroso compounds in acidic medium. Behavior of Ia was examined in hydrochloric acid-acetic acid, trifluoroacetic acid, boron trifluoride-dioxane and hydrochloric acid-ethanol. In each run conversion into N-(*p*-nitrosoanilinomethyl)succinimide (VII) proceeded at room temperature to a considerable extent as shown in Table VI. Thus, in acidic medium I was found to undergo migration of the nitroso group similar to the Fischer-Hepp migration,[3] the highest yield being obtained in hydrochloric acid-acetic acid medium.

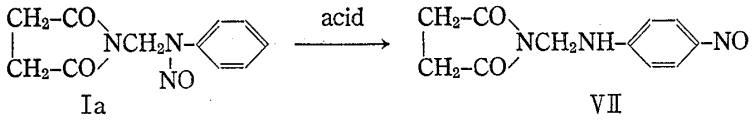
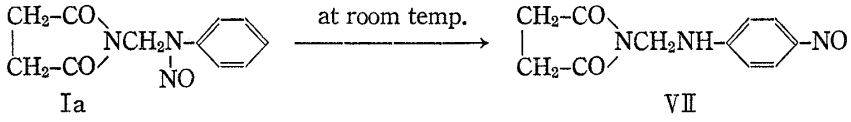


Table VI. Migration of Nitroso Group of Ia



Reaction condition	Reaction period (hr)	Yield (%)
HCl–AcOH	4	86
CF_3CO_2H	4	25
BF_3–dioxane	6	31
42% HCl–MeOH	5	47

5) R. Putter, "Methoden der Organischen Chemie," (Houben-Weyl), E. Muller, Bd. 10/3, Georg Thieme Verlag, Stuttgart, 1965, pp. 67—70.

N-[(N-Nitroso-*o*- and *m*-toluidino)methyl]succinimides (Ih and Ib) were also allowed to react in hydrochloric acid-acetic acid medium to give the corresponding *p*-nitrosoaniline derivatives in a good yield, but the N-nitroso compound derived from *p*-toluidine failed to undergo similar migration of the nitroso group, resulting in the formation of only a resinous material.

Experimental

All melting points are uncorrected. UV spectra were recorded on a Hitachi EPS-3T spectrophotometer. Infrared (IR) spectra were obtained with a Hitachi EPI-G2 spectrophotometer. NMR spectra were taken with a Hitachi R-24 spectrometer using tetramethylsilane (TMS) as internal standard.

N-[(N-Nitrosoarylamino)methyl]succinimides (I)——A solution of 0.12 mole of sodium nitrite in 30 ml of water was dropwise added to a stirred suspension of 0.1 mole of N-(arylaminomethyl)succinimide[4] in 200 ml of 2% HCl at room temperature. After the mixture was stirred for further 3 hr, resulted precipitates were collected by filtration and recrystallized from appropriate solvent. Yield, 65—80%. Spectral and analytical data of the nitroso products are listed in Tables I and II.

Azo-coupling Reactions of 2-Naphthol with I——To a solution of 0.02 mole of 2-naphthol in 20 ml of 10% aqueous NaOH 0.02 mole of powdered I was added. After the mixture was stirred at room temperature for 1.5—3 hr, most of the azo-coupling product deposited was collected by filtration. By acidification of the filtrate with acetic acid the additional amount of the product was obtained. Yields of the products are recorded in Table III. Physical and analytical data of the products are shown in the following.

1-Phenylazo-2-naphthol (IIa)——Dark purple prisms (acetone), mp 132—133° (lit.,[6] mp 132—133°). *Anal.* Calcd. for $C_{16}H_{12}ON_2$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.13; H, 5.03; N, 11.35.

1-(*p*-Tolylazo)-2-naphthol (IIb)——Orange needles (acetone), mp 132—134° (lit.,[6] mp 134—135°). *Anal.* Calcd. for $C_{17}H_{14}ON_2$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.46; H, 5.54; N, 10.55.

1-(*p*-Methoxyphenylazo)-2-naphthol (IIc)——Red needles (acetone), mp 134—136° (lit.,[7] 140°). *Anal.* Calcd. for $C_{17}H_{14}O_2N_2$: C, 73.36; H, 5.07; N, 10.07. Found: C, 73.03; H, 5.24; N, 10.03.

1-(*p*-Dimethylaminophenylazo)-2-naphthol (IId)——Blue black needles (acetone), mp 179—181° (lit.,[7] mp 180—182°). *Anal.* Calcd. for $C_{18}H_{17}ON_3$: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.19; H, 6.01; N, 14.72.

1-(*o*-Tolylazo)-2-naphthol (IIe)——Orange needles (acetone), mp 127—129° (lit.,[8] mp 130°). *Anal.* Calcd. for $C_{17}H_{14}ON_2$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.64; H, 5.58; N, 10.68.

1-(3-Pyridylazo)-2-naphthol (IIf)——Red plates (acetone), mp 145—146°. *Anal.* Calcd. for $C_{15}H_{11}ON_3$: C, 72.27; H, 4.45; N, 16.86. Found: C, 71.95; H, 4.34; N, 16.95.

Azo-coupling Reactions of Active Methylene Compounds with I——A mixture of 0.02 mole of active methylene compound (5,5-dimethyl-1,3-cyclohexanedione, 1,3-dimethylbarbituric acid and barbituric acid were used) in 20 ml of 10% aqueous NaOH and 0.02 mole of I was allowed to react in the same manner as described above. Reaction periods and yields of the products are recorded in Table IV. Spectral and analytical data of the products are shown in the following.

5,5-Dimethyl-2-(phenylhydrazono)-1,3-cyclohexanedione (IIIa)——Pale yellow plates (EtOH), mp 135—136° (lit.,[9] mp 142°). IR ν_{max}^{KBr} cm^{-1}: 1670, 1622 (C=O). NMR ($CDCl_3$) δ: 1.16 (6H, s, $2CH_3$), 2.60 (4H, s, $2CH_2$), 7.1—7.7 (5H, m, C_6H_5), 14.5 (1H, broad, NH). *Anal.* Calcd. for $C_{14}H_{16}O_2N_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.52; H, 6.56; N, 11.84.

1,3-Dimethyl-5-(phenylhydrazono)alloxane (IIIb)——Yellow granule (MeOH), mp 250—251° (lit.,[10] mp 258—259°). IR ν_{max}^{KBr} cm^{-1}: 1720, 1670, 1635 (C=O). NMR ($CDCl_3$) δ: 3.41 (3H, s) and 3.43 (3H, s, NCH_3), 7.2—7.7 (5H, m, C_6H_5), 14.5 (1H, broad, NH). *Anal.* Calcd. for $C_{12}H_{12}O_3N_4$: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.30; H, 4.69; N, 21.58.

5-(Phenylhydrazono)alloxane (IIIc)——Orange prisms (H_2O), mp 295—297° (lit.,[11] 298—300°). IR ν_{max}^{KBr} cm^{-1}: 1720, 1705, 1645 (C=O). *Anal.* Calcd. for $C_{10}H_8O_3N_4$: C, 51.72; H, 3.57; N, 24.13. Found: C, 51.71; H, 3.54; N, 23.68.

5,5-Dimethyl-2-(3-pyridylhydrazono)-1,3-cyclohexanedione (IIId)——Yellow prisms (EtOH), mp 176—178°. IR ν_{max}^{KBr} cm^{-1}: 1675, 1625 (C=O). NMR ($CDCl_3$) δ: 1.16 (6H, s, $2CH_3$), 2.12 (4H, s, $2CH_2$), 7.2—7.4, 7.8—8.2, 8.45—8.7 (4H, m, C_6H_4N), 15.2 (1H, broad, NH). *Anal.* Calcd. for $C_{13}H_{15}O_2N_3$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.63; H, 6.18; N, 17.15.

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1,3-Dimethyl-5-(3-pyridylhydrazono)alloxane (IIIe)——Yellow needles (MeOH), mp 235—237°. IR ν_{max}^{KBr} cm^{-1}: 1715, 1665, 1620 (C=O). NMR ($CDCl_3$) δ: 3.47 (3H, s), 3.49 (3H, s, NCH_3), 7.35—7.6, 8.0—8.4, 8.6—8.9 (4H, m, C_6H_4N), 14.5 (1H, broad, NH). *Anal.* Calcd. for $C_{11}H_{11}N_5O_3$: C, 50.57; H, 4.24; N, 26.81. Found: C, 50.49; H, 4.29; N, 27.05.

Reaction of N-[(N-Nitrosoanilino)methyl]succinimide (Ia) with Sodium Methoxide——A mixture of 2.3 g (0.01 mole) of Ia and 0.54 g (0.01 mole) of sodium methoxide in 10 ml of MeOH was stirred at 40—45° until the evolution of nitrogen gas ceased. The mixture was added with 8 ml of 5% HCl followed by concentration under reduced pressure. The residue was extracted with ether and the ether solution was dried over $MgSO_4$. Removal of ether gave an oily residue, which was distilled under reduced pressure to give a solid distillate, bp 80—85° (0.5 mmHg) and mp 67—68°. This product was identified as biphenyl by comparison of its IR spectrum with that of authentic specimen. Yield, 0.36 g (50%).

Reactions of I with Secondary Amines——A mixture of 0.02 mole of I and 15 ml of piperidine, pyrrolidine or morpholine was heated at reflux until a spot of the starting material was not observed on thin layer chromatogram. The reaction mixture was evaporated under reduced pressure to remove excess secondary amine followed by extraction with ether. The ether solution was dried over $MgSO_4$ and concentrated. The residual oily or crystalline material was purified by distillation under reduced pressure or recrystallization from appropriate solvent and identified as triazene.

The ether insoluble substance was recrystallized to give crystals of V, yields of which were 70—80%. Reaction periods and yields of triazenes are recorded in Table V. Spectral and analytical data of the products are shown in the following.

1-Phenylazopiperidine (IVa)——bp 97—101° (0.05 mmHg). prisms (petr. ether), mp 44—45° (lit.,[12] mp 42°). NMR ($CDCl_3$) δ: 1.63—1.85 (6H, m, $-CH_2CH_2CH_2-$), 3.34—3.94 (4H, m, $-CH_2NCH_2-$), 6.8—7.5 (5H, m, C_6H_5). *Anal.* Calcd. for $C_{11}H_{15}N_3$: C, 69.81; H, 7.99; N, 22.20. Found: C, 69.87; H, 8.03; N, 22.41.

1-Phenylazopyrrolidine (IVb)——Prisms (AcOEt), mp 48—49° (lit.,[13] mp 49—50), NMR ($CDCl_3$) δ: 1.8—2.2 (4H, m, $-CH_2CH_2-$), 3.6—4.0 (4H, m, $-CH_2NCH_2-$), 7.0—7.5 (5H, m, C_6H_5). *Anal.* Calcd. for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.41; H, 7.47; N, 24.36.

4-Phenylazomorpholine (IVc)——bp 126—128° (0.08 mmHg), mp 28—29° (lit.,[14] mp 29—30°). NMR ($CDCl_3$) δ: 3.75 (8H, s, morpholine ring protons), 7.1—7.6 (5H, m, C_6H_5). *Anal.* Calcd. for $C_{10}H_{13}ON_3$: C, 62.80; H, 6.85; N, 21.98. Found: C, 62.99; H, 6.93; N, 22.04.

1-(*p*-Tolylazo)piperidine (IVd)——bp 96—98° (0.04 mmHg), prisms (petr. ether), mp 43—45° (lit.,[15] mp 41°). NMR ($CDCl_3$) δ: 2.26 (3H, s, CH_3), 1.55—1.75 (6H, m, $-CH_2CH_2CH_2-$), 3.42—3.91 (4H, m, $-CH_2NCH_2-$), 6.94 (2H, d) and 7.19 (2H, d, aromatic protons). *Anal.* Calcd. for $C_{12}H_{17}N_4$: C, 70.90; H, 8.43; N, 20.67. Found: C, 71.07; H, 8.44; N, 20.96.

1-(2-Pyridylazo)piperidine (IVe)——bp 121—124° (0.25 mmHg), prisms ($(C_2H_5)_2O$), mp 51—52°. NMR ($CDCl_3$) δ: 1.5—1.9 (6H, m, $-CH_2CH_2CH_2-$), 3.7—4.1 (4H, m, $-CH_2NCH_2-$), 6.9—7.8 (3H, m, 3,4,5-H), 8.5 (1H, d, 6-H). *Anal.* Calcd. for $C_{10}H_{14}N_4$: C, 63.13; H, 7.42; N, 29.45. Found: C, 63.22; H, 7.50; N, 29.75.

1-(3-Pyridylazo)piperidine (IVf)——bp 140—141° (0.01 mmHg). NMR ($CDCl_3$) δ: 1.4—1.9 (6H, m, $-CH_2CH_2CH_2-$), 3.6—4.0 (4H, $-CH_2NCH_2-$) 7.25 (1H, dd, 5-H), 7.75 (1H, td, 4-H), 8.43 (1H, dd, 6-H), 8.75 (1H, d, 2-H). *Anal.* Calcd. for $C_{10}H_{14}N_4$: C, 63.13; H, 7.42; N, 29.45. Found: C, 62.78; H, 7.46; N, 26.35.

1-Piperidino-N-(1-piperidinomethyl)-γ-oxobutyramide——Needles (AcOEt), mp 118—119°. IR ν_{max}^{KBr} cm^{-1}: 3289 (NH), 1669, 1621 (C=O). NMR ($CDCl_3$) δ: 1.3—2.8 (12H, m, $2\times-CH_2CH_2CH_2-$), 2.15—2.75 (8H, m, $-CH_2CH_2-$, $-CH_2NCH_2-$), 3.15—3.70 (4H, m, $-CH_2NCH_2-$), 4.54 (2H, d, $N-CH_2-N$), 5.17 (1H, broad, NH). *Anal.* Calcd. for $C_{15}H_{27}O_2N_3$: C, 64.02; H, 9.67; N, 14.93. Found: C, 64.13; H, 9.72; N, 15.04.

1-Pyrrolidino-N-(1-pyrrolidinomethyl)-γ-oxobutyramide——Prisms (AcOEt), mp 131—132°. IR ν_{max}^{KBr} cm^{-1}: 3288 (NH), 1662, 1621 (C=O). NMR ($CDCl_3$) δ: 1.5—2.2 (8H, m, $2\times-CH_2CH_2-$), 2.4—2.8 (8H, m, $-CH_2CH_2-$, $-CH_2NCH_2-$), 3.49 (4H, *ca.* t, $-CH_2NCH_2-$), 4.19 (2H, d, $N-CH_2-N$), 7.0 (1H, broad, NH). *Anal.* Calcd. for $C_{13}H_{23}O_2N_3$: C, 61.64; H, 9.14; N, 16.48. Found: C, 61.63; H, 9.15; N, 16.59.

4-Morpholino-N-(4-morpholinomethyl)-γ-oxobutyramide——Prisms (EtOH), mp 148—149°. IR ν_{max}^{KBr} cm^{-1}: 3295 (NH), 1672, 1628 (C=O). NMR ($CDCl_3$) δ: 2.4—2.8 (8H, m, $-CH_2CH_2-$, $-CH_2NCH_2-$), 3.4—4.0 (12H, m, $2\times-CH_2OCH_2-$, $-CH_2NCH_2-$), 4.10 (2H, d, $N-CH_2-N$), 6.6 (1H, broad, NH). *Anal.* Calcd. for $C_{13}H_{23}O_4N_3$: C, 54.72; H, 8.13; N, 14.73. Found: C, 54.48; H, 7.93; N, 14.54.

In the above reaction of I with morpholine usual treatment of the reaction solution after 3 hr's refluxing gave 4-morpholino-N-([N-nitrosoanilino)methyl]-γ-oxobutyramide. Yield, 84%. Needles (EtOH), mp 115—116°. IR ν_{max}^{KBr} cm^{-1}: 3295 (NH), 1675, 1630 (C=O). NMR ($CDCl_3$) δ: 2.5—2.8 (4H, m, $-CH_2CH_2-$), 3.4—3.7 (8H, m, morpholine ring protons), 5.3 (2H, d, $N-CH_2-N$), 7.2 (1H, broad, NH), 7.3—7.9 (5H, m, C_6H_5). *Anal.* Calcd. for $C_{15}H_{20}O_4N_4$: C, 56.24; H, 6.29; N, 17.49. Found: C, 56.31; H, 6.27; N, 17.48.

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This compound was again refluxed in morpholine for further 5 hr to give IVc and 4-morpholino-N-(morpholinomethyl)-γ-oxobutyramide.

Reactions of I in Acid Media——1) In HCl–AcOH Medium: To a solution of I in 20 ml of AcOH 4 ml of 35% HCl was dropwise added with stirring. After the addition was completed, stirring at room temperature was continued for 3 hr. The solution was diluted with ice-cold water and neutralized with ammonia on cool to give powder, which was collected by filtration and dried. This was identified as N-(*p*-nitrosoarylaminomethyl)succinimide, as in the following.

N-(*p*-Nitrosoanilinomethyl)succinimide (VII)——Yield, 86%. Green prisms (acetone), mp 188—189° (lit.,[16] mp 189—189.5°). IR ν_{max}^{KBr} cm^{-1}: 3320 (NH), 1764, 1697 (C=O), 830 (δCH). *Anal.* Calcd. for $C_{11}H_{11}O_3N_3$: C, 64.05; H, 3.49; N, 14.94. Found: C, 64.15; H, 4.20; N, 14.90.

N-(*p*-Nitroso-*o*-toluidinomethyl)succinimide——Yield, 92%. Green prisms (acetone), mp 143—144°. IR ν_{max}^{KBr} cm^{-1}: 3374 (NH), 1779, 1697 (C=O), 893, 819 (δCH). *Anal.* Calcd. for $C_{12}H_{13}O_3N_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.28; H, 5.38; N, 16.93.

N-(*p*-Nitroso-*m*-toluidinomethyl)succinimide——Yield, 92%. Green needles (acetone), mp 172—173°. IR ν_{max}^{KBr} cm^{-1}: 3327 (NH), 1771, 1698 (C=O), 878, 826 (δCH). *Anal.* Calcd. for $C_{12}H_{13}O_3N_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.29; H, 5.36; N, 16.89.

2) In Trifluoroacetic Acid Medium: A mixture of 4.6 g (0.02 mole) of Ia and 5 ml of trifluoroacetic acid was stirred at room temperature for 4 hr. The reaction mixture was treated by the same manner as 1) to give VII. Yield, 1.15 g (25%).

3) In BF_3-dioxane Medium: Into a suspension of 2.3 g (0.01 mole) of Ia in 10 ml of dioxane 7 ml of 47% boron fluoride etherate was added. The mixture was stirred at room temperature for 6 hr and treated by the same manner as 1) to give VII. Yield, 0.7 g (31%).

4) In HCl–EtOH Medium: A suspension of 2.3 g (0.01 mole) of Ia in 20 ml of 42% HCl–EtOH was stirred at 10—15° for 5 hr. The reaction mixture was treated by the same manner as 1) to give VII. Yield, 1.1 g (47%).

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