sodium hydride in 100 ml of 1,2-dimethoxyethane kept at a temperature below 10°. Upon cessation of gas evolution, 1-methyl-3-piperidone, liberated from 4.08 g of its hydrochloride,[24] was added dropwise to the mixture still below 10°. The mixture then was stirred at 0° for 5 min and at room temperature for 1.3 hr. Saturated brine solution (80 ml) was added and the homogeneous solution extracted exhaustively with ether. The extract was dried over sodium sulfate and evaporated. Distillation of the residue gave 3.10 g of liquid methyl 1-methyl-3-carbomethoxymethylenepiperidine (XX, R = Me): bp 71–72° (0.5 mm); infrared (neat) C=O 5.83 (s), C=C 6.06 μ (s); ultraviolet λ_{max}^{EtOH} 214 mμ (ε 15,500); the pmr spectrum showed two three-proton singlets at 2.23 and 2.26 (N—Me of both stereoisomers), a three-proton singlet at 3.62 (O—Me), and a one-proton multiplet at 5.62 (olefinic H); gpc (F & M Model 500, *vide supra*) retention time 223 sec. Its treatment with a saturated solution of picric acid in 95% ethanol and crystallization of the product from ethanol yielded yellow needles of XX (R = Me) picrate: mp 148°; infrared spectrum (Nujol) NH^+ 3.7 (m, broad), C=O 5.87 (s), C=C 6.03 (m), 6.14 (s), 6.21 μ (s).

Anal. Calcd for $C_{15}H_{18}O_9N_4$: C, 45.23; H, 4.55; N, 14.07. Found: C, 45.39; H, 4.84; N, 14.16.

The product mixture from the sodium methoxide treatment of XX (R = Me) (*vide infra*) was treated with a saturated solution of picric acid in 95% ethanol. Repeated fractional crystallization of the mixture of solids from ethanol separated the highest melting picrate. The latter was decomposed in 10% sodium hydroxide solution and the free base taken up in methylene chloride. The organic solution was dried over sodium sulfate and evaporated. The liquid product, methyl 1-methyl-3-methoxyhomonipecotate (XXI) (the infrared spectrum (neat) showed C=O at 5.70 μ (s); the pmr spectrum showed three-proton singlets at 2.25 (N—Me), 3.29 (ether O—Me), 3.69 (ester O—Me) and a two-proton singlet at 2.58 ppm (exocyclic methylene)), was reconverted to its picric acid derivative: mp 180–181°; infrared spectrum (Nujol) NH^+ 3.7 (m), C=O 5.78 (s), C=C 6.10 (s), 6.14 (s), 6.17 (s), 6.21 μ (s).

Anal. Calcd for $C_{16}H_{22}O_{10}N_4$: C, 44.65; H, 5.15; N, 13.02. Found: C, 44.67; H, 5.13; N, 12.96.

Interconversion of XVIId and XVIIe.—With high material recovery as a constant goal a variety of conditions of the reaction of each of the esters with sodium methoxide in methanol was tested (changes in concentration of ester and of base, in temperature and in time). The reactions were monitored and the product ratios determined by pmr and gpc methods (*vide supra*). The best reaction conditions were found to be the following. The ester was added to a *ca.* 1% sodium methoxide (*ca.* 65 mole %) solution in methanol and the mixture refluxed under nitrogen for 2 hr. Water was added to the cooled solution and the mixture extracted with methylene chloride. The extract was dried over sodium sulfate and evaporated under vacuum. The residual oil then was analyzed for product content.

Registry No.—Ia, 14997-23-0; Ib, 14996-82-8; Ic, 15083-66-6; Id, 14996-83-9; Il, 14996-84-0; If, 14996-85-1; Ig, 14996-86-2; Il (X = Br), 14996-87-3; Il (X = ClO_4), 14996-88-4; Im, 14996-89-5; IIa, 14996-90-8; IIb, 14996-91-9; IIc, 14996-92-0; IId, 14996-93-1; IIe, 14996-94-2; IIf, 14996-95-3; IIg, 15077-09-5; IIk, 14996-96-4; IIi, 14996-97-5; IIj, 14996-98-6; IIk, 14996-99-7; IIIb, 14997-00-3; IV, 14997-01-4; VI, 14997-02-5; VII, 14997-03-6; XIb, 14997-04-7; XIc, 14997-05-8; XIe, 7032-11-3; XIIa, 14997-07-0; XIIb, 15083-67-7; XIIId, 14997-08-1; XIIIe, 14997-09-2; XIIIf, 14997-10-5; XIII (R = H, R′ = CO_2Me, R″ = Cl = CH_2CO), 14996-76-0; XIII (R = CH_2CO_2Me, R′ = CO_2Me, R″ = $ClCH_2$-CO), 15076-94-5; XIII (R = CH_2CO_2Me, R′ = CO_2Me, R″ = Ac), 14996-77-1; XVIa, 14997-11-6; XVIb, 14997-12-7; XVIIb, 14997-13-8; XVIIc, 14997-14-9; XVIId, 14997-15-0; XVIId picrate, 14997-16-1; XVIIe picrate, 14997-17-2; XX (*trans*), 14997-18-3; XX (*trans*) picrate, 14997-19-4; XX (*cis*), 14997-21-8; XX (*cis*) picrate, 14997-22-9; XXI, 15077-10-8; XXI picrate, 14997-20-7; β-hydroxymethylpyridine, 586-98-1.

The Kinetics of *syn–anti* Conversions of 2,4-Dinitrophenylhydrazones[1]

A. F. HEGARTY AND F. L. SCOTT

Chemistry Department, University College, Cork, Ireland

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The kinetics of bromination of alkylidene 2,4-dinitrophenylhydrazones (DNPs) (giving the corresponding alkylhydrazidic bromides) were studied using an electrometric technique to follow the low (*ca.* 10^{-5} *M*) bromine concentrations involved. The reaction was zero order in bromine. It was also insensitive to variation in the halogenating species (as between, *e.g.*, bromine, tribromide ion, and chlorine). The first-order rate constants for the reactions of eight alkylidene DNPs were correlated by the Taft equation with $\delta = +0.49$; *i.e.*, the rate of internal hydrazone change measured was dependent only on the size of the alkyl group involved. This was interpreted in terms of rate-determining *syn–anti* isomerism. Consistent with this proposal, bromination of N-(2,4-dinitrophenyl)-2-pyrazoline, which is a model for the *anti* isomer of the DNP, was a rapid second-order reaction. The preparation of a DNP with an asymmetric center α to the bromination site was achieved and its bromination occurred with essentially complete retention of optical activity. This, together with some chemical evidence, makes ene–hydrazine formation as the slow step unlikely (although this may be the rate-determining step with ketone DNPs). Rate data implied that N,N-disubstituted hydrazones, which are widely reported as being inactive toward electrophilic attack, should be brominated, though at a much reduced rate. An N,N-disubstituted hydrazidic bromide has been isolated for the first time from the bromination of one of the appropriate hydrazones and was readily converted into the corresponding hydrazide. We regard normal electrophilic substitution of arylidene (or alkylidene)hydrazones as SE2′ reactions and the corresponding reactions of N,N-disubstituted hydrazones as SE2 processes. The hydrolysis of the eight alkylhydrazidic bromides isolated (by bromination of the alkylidene DNPs), together with some of their reactions with nucleophiles, are also described.

Although 2,4-dinitrophenylhydrazine has been widely recommended as a reagent for the characterization of carbonyl compounds, its use for the formation of derivatives of simple aldehydes has been restricted because of the often widely differing melting points reported for these compounds. These differences in melting points have been variously ascribed to the coexistence of two (or more) isomeric forms of the hydrazones involving either geometric isomers (*syn* and *anti*) about the azomethine bond (—C=N—) or

(1) Some of the results reported here have been presented in communication form: A. F. Hegarty and F. L. Scott, *Chem. Commun.*, 521 (1967).

tautomeric forms of the hydrazone (ene–hydrazine and azoalkane species).[2] Karabatsos and coworkers[3] in a recent study using nmr techniques failed to detect either the ene–hydrazine or azoalkane tautomers of 2,4-dinitrophenylhydrazones (DNPs) in solution, thus contradicting the earlier work of O'Connor.[4] But DNPs were shown to equilibrate in solution to mixtures of *syn* and *anti* isomers and this equilibration occurred most readily in the presence of acid.[3a] We have now examined the bromination of these hydrazones and have found that both the kinetic equations and structural effects are quite different for these DNPs (compared with the arylidene hydrazones we studied previously[5]) and that the present results can best be described in terms of the interconversion of *syn* and *anti* hydrazone forms in solution.

Results and Discussion

The bromination of arylidene arylhydrazones, I, leads to the replacement of the methine hydrogen and the formation of hydrazidic bromides, II (see eq 1).

$$\underset{\text{I}}{\text{RCH=NNHAr}} \xrightarrow{\text{Br}_2} \underset{\text{II}}{\text{RCBr=NNHAr}} \qquad (1)$$

Ia, IIa, Ar = 2,4-$(NO_2)_2C_6H_3$

In this reaction derivatives of a variety of substituted hydrazines have been used (*e.g.*, tetrazolylhydrazones,[6] semicarbazones,[7] 2-pyridylhydrazones,[8] carbethoxyhydrazones,[9] and phenylhydrazones[10]) but the arylidene component has previously been restricted to substituted phenyl. We have now extended this reaction to alkylidene hydrazones and have found that bromination of these hydrazones (Ia, R = alkyl) in acetic acid gives the corresponding alkylhydrazidic bromides (IIa, R = alkyl) in high yield.

We have studied the kinetics of this process in 70% acetic acid containing 0.1 *M* potassium bromide using a polarized rotating platinum electrode[5] to measure low bromine concentrations involved. It has been well established, mainly by the work of Berliner and coworkers,[11] that in this solvent mixture the active brominating species are molecular bromine and tribromide ion and simple kinetic equations result; dependence on high powers of the bromine concentration, found almost invariably in glacial acetic acid,[12] being negligible. We have confirmed this earlier in our own study of the bromination of substituted benzylidene *p*-nitrophenylhydrazones (I, R = XC_6H_4, Ar = *p*-$NO_2C_6H_4$) which were shown to follow the simple second-order kinetic equation[5]

$$-\frac{d[Br_2]}{dt} = k([Br_2] + [Br_3^-])(\text{hydrazone})$$

When the rate of bromination of acetaldehyde DNP (Ia, R = CH_3) was studied under these conditions, it was found that, surprisingly, the bromine concentration fell linearly with time. Data from several experiments at various initial concentrations of bromine and the DNP showed that the over-all reaction was first order in hydrazone and zero order in bromine, *i.e.*, the rate law followed was

$$v = -\frac{d[Br_2]}{dt} = k_1[\text{hydrazone}]$$

To discover how general a phenomenon this was, the bromination of seven other alkylidene DNP's was studied (Table I). All showed the same behavior in that the reaction was zero order in halogen, but the first-order k_1 values obtained varied with the hydrazone used. From the data (Table I) it is clear that simple electronic effects alone do not influence the reactivity of the hydrazones. Thus trimethylacetaldehyde DNP reacted at about the same rate as dichloroacetaldehyde DNP (both compounds reacting much more slowly than acetaldehyde DNP) even though electronic effects would be expected to operate in opposite directions in these two compounds. The rate data were correlated with a high degree of precision by the reduced form of the Taft equation:[13] $\log k = \delta E_S + \log k_0$, from which a δ value of +0.49 was obtained with $r = 0.996$, $s = 0.04$ and $\log k_0$ (CH_3) = −2.53 (Figure 1). This implies that steric effects alone account best for the difference in reactivity between the various hydrazones, electronic effects (within the precision of the E_S values used) being negligible (*i.e.*, $\rho^* = 0$).

TABLE I
RATES OF BROMINATION OF ALKYLIDENE 2,4-DINITROPHENYLHYDRAZONES ($RCH{=}NNHC_6H_3(NO_2)_2$) AT 20° IN 70% ACETIC ACID

R–	CH_3	CH_3CH_2	$(CH_3)_2CH$	$C_2H_5(CH_3)CH$
10^4k_1[a]	31.1	29.3	15.6	9.0
R–	$(CH_3)_3C$	$C_6H_5CH_2$	$ClCH_2$	Cl_2CH
10^4k_1[a]	5.4	18.7	21.5	5.1

[a] In sec^{-1}; each is an average result from three to six experiments.

The bromination of one of the hydrazones, isobutyraldehyde DNP, was studied under conditions where the Br_2:Br_3^- ratio varied considerably, the ionic strength being maintained constant at 0.1 *M* by the addition of potassium nitrate. The rate constants (k_1 values) obtained (Table II) were found to be essentially independent of the bromide ion con-

(2) (a) M. E. Umstead, Ph.D. Thesis, Pennsylvania State University, State College, Pa.,[1] 1957; (b) C. K. Ingold, G. J. Pritchard, and H. G. Smith, *J. Chem. Soc.*, 70 (1934); W. M. D. Bryant, *J. Am. Chem. Soc.*, **60**, 70 (1934); F. Ramirez and A. F. Kirby, *ibid.*, **76**, 1037 (1954).

(3) (a) G. J. Karabatsos, F. M. Vane, R. A. Taller, and N. Hsi, *ibid.*, **86**, 3351 (1964); (b) G. J. Karabatsos, R. A. Taller, and F. M. Vane, *Tetrahedron Letters*, 1081 (1964); (c) G. J. Karabatsos and R. A. Taller, *J. Am. Chem. Soc.*, **85**, 3624 (1963); G. J. Karabatsos, B. L. Shapiro, F. M. Vane, J. S. Fleming, and J. S. Ratka, *ibid.*, **85**, 2784 (1963).

(4) R. O'Connor, *J. Org. Chem.*, **26**, 4375 (1961); R. O'Connor and W. Rosenbrook, *ibid.*, **26**, 5208 (1961); R. O'Connor and G. Henderson, *Chem. Ind.* (London), 850 (1965).

(5) (a) A. F. Hegarty and F. L. Scott, *J. Chem. Soc., Sect. B*, 672 (1966); (b) 1031 (1966).

(6) R. N. Butler and F. L. Scott, *J. Chem. Soc., Sect. C*, 239 (1967); F. L. Scott and D. A. Cronin, *Tetrahedron Letters*, 715 (1963).

(7) M. S. Gibson, *Tetrahedron*, **18**, 1377 (1962); H. Gehlen and K. Mockel, *Ann.*, **651**, 133 (1962); H. Najer, R. Gindicelli, C. Morel, and J. Menin, *Bull. Soc. Chim. France*, 153 (1966).

(8) M. S. Gibson, *Tetrahedron*, **19**, 1587 (1963).

(9) T. Bacchetti, *Gazz. Chim. Ital.*, **91**, 866 (1961).

(10) F. D. Chattaway and A. J. Walker, *J. Chem. Soc.*, 975 (1925).

(11) E. Berliner and M. C. Beckett, *J. Am. Chem. Soc.*, **79**, 1425 (1957); U. P. Zimmerman and E. Berliner, *ibid.*, **84**, 3952 (1962); E. Berliner and B. J. Landry, *J. Org. Chem.*, **27**, 1083 (1962); L. Altschuler and E. Berliner, *J. Am. Chem. Soc.*, **88**, 5837 (1966).

(12) P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworth and Co. Ltd., London, 1959, Chapter 9; R. M. Keefer and L. J. Andrews, *J. Am. Chem. Soc.*, **78**, 3637 (1956).

(13) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newmann, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 598.

TABLE II
RATE CONSTANTS FOR THE BROMINATION OF ISOBUTYRALDEHYDE DNP IN 70% ACETIC ACID AT 20° [a]

[KBr], mole l.$^{-1}$	[KNO_3], mole l.$^{-1}$	10^3k_1, sec^{-1} [b]
0.10	0.00	1.56
0.05	0.05	1.54
0.04	0.06	1.59
0.03	0.07	1.58
0.02	0.08	1.64
0.01	0.09	1.64

[a] Each is an average result of three experiments. [b] Mean value = (1.59 ± 0.03) × 10^{-3} sec^{-1}.

centration used. Since bromine and tribromide ion are reagents of different electrophilic strengths,[14] the fact that the rate constant for the hydrazone remains unchanged when their relative amounts present change by a factor of about ten adds support to the view that the electrophile is not involved in the rate-determining step of the reaction. Moreover the rate of chlorination of isobutyraldehyde DNP was approximately the same as the rate of bromination (k_1 = (1.6 ± 0.3) × 10^{-3} sec^{-1}). Although the chlorination rates could not be determined to the same degree of accuracy as the bromination rates since the concentration *vs.* time plots were curved,[15] the fact that there is no appreciable difference between the rates of chlorination and of bromination also supports the idea that the process being measured does not involve a rate-determining reaction between hydrazone and halogenating species.

The rate-controlling step therefore involves the hydrazone alone. This step could be the conversion of an unreactive form of the hydrazone present in excess, to a more reactive form (hydrazone'), the latter reacting relatively rapidly with bromine. This would give the reaction scheme

$$\text{hydrazone} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{hydrazone}'$$

$$\text{hydrazone}' + Br_2 \xrightarrow{k_2} \text{hydrazone Br} + Br^- + H^+$$

Applying the steady-state assumption for the concentration of hydrazone', the following expression is obtained for the reaction velocity (Br_2* represents [Br_2] + [Br_3^-]).

$$v = -\frac{d[Br_2^*]}{dt} = \frac{k_2k_1[Br_2^*][\text{hydrazone}]}{k_{-1} + k_2[Br_2^*]}$$

For a given system, *i.e.*, with k_{-1} and k_2 fixed, then with sufficiently high bromine concentration k_2. [Br_2*] $\gg k_{-1}$, the rate expression will reduce to

$$v = -d[Br_2^*]d/t = k_1[\text{hydrazone}]$$

As we have indicated this was the experimentally determined rate law followed in the bromination of alkylidene DNPs. At much lower bromine concentrations a situation might arise where $k_{-1} \gg k_2[Br_2^*]$, and then

$$v = -d[Br_2^*]d/t = k_2k_1/k_{-1}[Br_2^*][\text{hydrazone}]$$

i.e., the reaction would then become first order both in bromine and hydrazone. Whether this condition can be reached depends on the magnitudes of k_1/k_{-1}, *i.e.*,

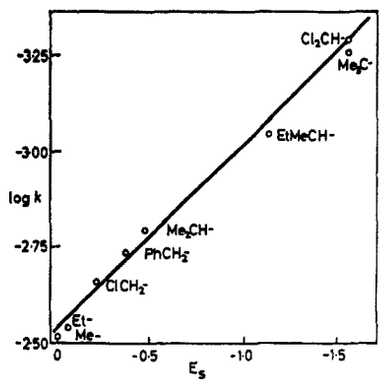
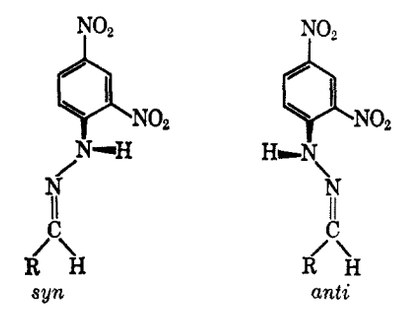


Figure 1.—Taft plot of log k for the bromination of alkylidene DNPs (Ia, R = alkyl) against the steric substituent constants, E_s.

the equilibrium constant for the formation of hydrazone', and k_2, the second-order rate constant for the reaction of hydrazone' with bromine. Attempts were made to achieve this situation for acetaldehyde DNP by using initial bromine concentrations as low as 10^{-6} M, but the reaction remained zero order in bromine.

As shown above, the magnitude of the k_1 values obtained depends essentially on the size of the alkyl group involved, the rate of conversion of hydrazone → hydrazone' decreasing as a more bulky R group is introduced. These data are consistent with a rate-determining conversion of the *syn* isomer of the hydrazone to the reactive *anti* isomer. In all cases the *syn* form is thermodynamically favored over the *anti*[3] because of interaction between the dinitroanilino



and R groups in the *anti* isomer. If the *anti* isomer were to be brominated at a far higher rate than the *syn* isomer, for example, for steric reasons since the dinitroanilino group lies close to the methine hydrogen in the *syn* isomer, then the reaction being measured could be the rate of *syn–anti* isomerism. The *anti* isomer has a *cis* configuration and kinetic studies have shown that bromination of olefins in this configuration (relative to the *trans* isomer) is always more rapid and the rate differences in some cases may be appreciable, (k_{cis}/k_{trans} for the stilbenes can be approximately 12).[16]

Moreover N-methylation of the hydrazone has been shown to reduce the concentration of the *anti* isomer to such an extent that it cannot be detected spectroscopically.[3b] Consistent with this we have found that the k_1 values for the bromination of such hydrazones were 17–27 times smaller (Table III) than for the corresponding reaction with the unmethylated hydrazones.

(14) R. P. Bell and M. Pring, *J. Chem. Soc., Sect. B*, 1119 (1966).
(15) Similar curved plots in bromination reactions were obtained by R. P. Bell and K. Yates, *J. Chem. Soc.*, 362 (1962).
(16) J. E. Dubois and G. Mouvier, *Tetrahedron Letters*, 1629 (1965); R. E. Buckles, J. L. Miller, and R. J. Thurmaier, *J. Org. Chem.*, **32**, 888 (1967).

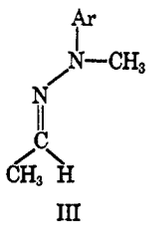
TABLE III

RATE CONSTANTS FOR BROMINATION OF DNPs ($R_1R_2C{=}NNR_3C_6H_3(NO_2)_2$) AT 20° IN 70% ACETIC ACID CONTAINING 0.1 *M* Br^-

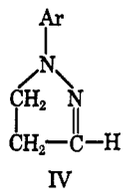
R_1	R_2	R_3	10^4k_1, sec^{-1}	k_H/k_{CH_3}
CH_3	H	H	31.1	
CH_3	H	CH_3	1.8	17
$(CH_3)_2CH$	H	H	15.6	
$(CH_3)_2CH$	H	CH_3	0.8	20
$(CH_3)_3C$	H	H	5.4	
$(CH_3)_3C$	H	CH_3	0.2	27
CH_3	CH_3	H	32.0	
CH_3	CH_3	CH_3	48.0	0.67
$C_6H_5CH_2$	CH_3	H	11.8	
$C_6H_5CH_2$	CH_3	CH_3	25.0	0.47

1-(2′,4′-Dinitrophenyl)-2-pyrazoline (IV, Ar = 2,4-$(NO_2)_2C_6H_3$) constitutes a model for the *anti* configuration of the hydrazone and was brominated to give a 3-bromopyrazoline analogous to a hydrazidic bromide. The bromination reaction is a rapid second-order (k_2 = 10 l. $mole^{-1}$ sec^{-1}) process, first order each in pyrazoline and bromine. This information first of all indicates the likely order of magnitude for the k_2 values involved in the brominations of the alkylidene DNPs. Furthermore, inasmuch as the bromination rate of the substituted pyrazoline (our model for the *anti* hydrazone tautomer) is first order in both bromine and the hydrazone, then it seems likely that the bromination of the *syn* isomer, while slower, is also a second-order process, first order again in bromine and hydrazone. The fact that the bromination reactions of the alkylidene DNPs are zero order in bromine then confirms that in these reactions we are not measuring kinetically a hydrazone bromination reaction but instead a prebromination transformation.

Although our data permit the accurate calculation of k_1 values (for *syn* to *anti* conversion), we cannot in fact obtain exact *syn–anti* equilibration ratios. These can, however, be estimated since the kinetic equation followed requires that $k_2[Br_2] \gg k_{-1}$. For acetaldehyde N-MeDNP (III, Ar = 2,4-$(NO_2)_2C_6H_3$) if the k_2 value is assumed to be *ca.* 10 l. $mole^{-1}$ sec^{-1} (the value



III

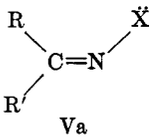


IV

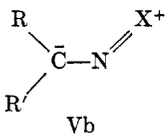
obtained with the pyrazoline model) then with $[Br_2] = 10^{-5}$ mole $l.^{-1}$, a k_1/k_{-1} value, the *syn–anti* equilibrium constant, of not greater than 10^{-2} is obtained. Thus our data predicts that less than 1% of the *anti* isomer of this N-MeDNP is present at equilibrium. This is consistent with the observation that the *anti* isomer of such N,N-disubstituted hydrazones is present in such small amounts that they have not been detected using the nmr technique.[3b]

The *syn–anti* isomer equilibrium ratios quoted by Karabatsos[3] for alkylidene DNPs are higher than would be predicted from the bromination reaction (although, as explained above, the order is the same). The *syn–anti* ratios were obtained by Karabatsos in methylene bromide solution, and when the dielectric constant of the medium was raised, a new equilibrium was established with larger amounts of the *syn* form present (*e.g.*, for acetaldehyde DNP, the equilibrium changed by a factor of 3 in going from methylene bromide to dimethyl sulfoxide). The medium effect is probably sufficiently large to explain the small equilibrium constants which we calculate (for 70% acetic acid containing 0.1 *M* bromide ion).

The uncatalyzed *syn–anti* isomerism of imines, oxime ethers, and halimines has recently been studied by Curtin and coworkers.[17] They reported



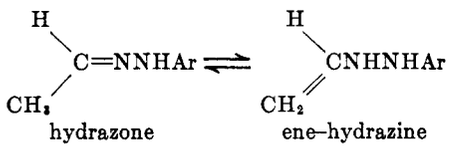
Va



Vb

that the k_1 values for *syn–anti* isomerism varied widely with the nature of X (over at least 16 powers of 10). When the group X had an unshared electron pair (*e.g.*, X = OH, OR, halogen), the rates of isomerism were far slower than when X = CH_3 or Ph, making it unlikely that isomerism occurs *via* a reaction pathway involving fission of the —C=N— π bond (which would be facilitated by the contribution of structures such as Vb) and an alternative "lateral shift" mechanism has been proposed. This involves the shift of the group X from one side of the molecule to the other through a linear transition state. Although our results, with k_1 values for *syn–anti* isomerism when X = $NHC_6H_3(NO_2)_2$ in the region 10^{-3} to 10^{-4} sec^{-1} are about of the order of magnitude expected from the data presented by Curtin,[17] since our reaction conditions differ markedly from theirs a clearer comparison cannot be made.

One of the most obvious differences between the alkylidene DNPs and arylidene arylhydrazones (whose rate of bromination depends on the bromine concentration[5]) is that the latter are not capable of tautomerizing to the ene–hydrazine form. The existence of this type of isomerism (eq 2), occurring to



hydrazone ene–hydrazine (2)

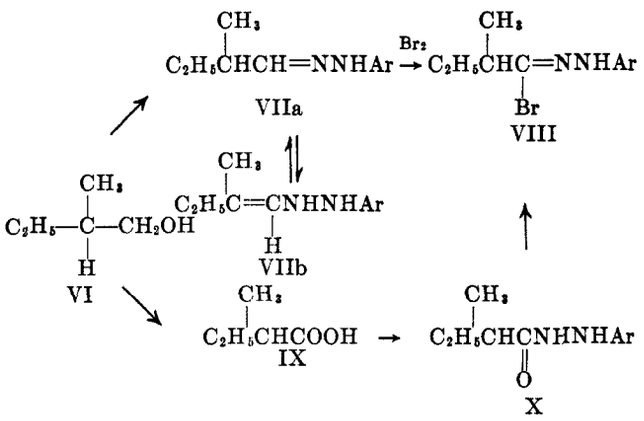
a small extent and giving an ene–hydrazine which was then rapidly brominated, could also explain the observed kinetics, but the results from a number of experiments make ene–hydrazine formation unlikely as the rate-determining step in the bromination of alkylidene DNPs.

It was shown by using an alkylidene DNP with an asymmetric carbon α to the bromination site that methine bromination was occurring without ene–hydrazine formation. Optically active 2-methylbutyraldehyde DNP (VII) was brominated to give the hydrazidic bromide VIII which was also optically active (see Scheme I). It has been long established[18]

(17) D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, *J. Am. Chem. Soc.*, **88**, 2775 (1966).

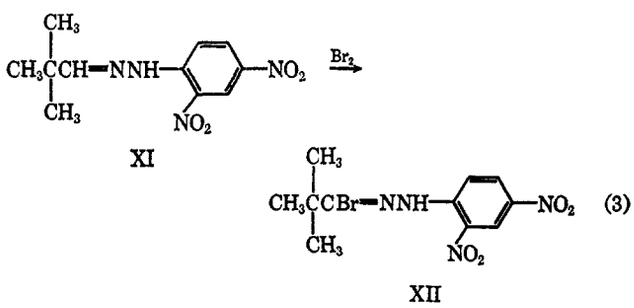
(18) A. Lapworth, *J. Chem. Soc.*, 30 (1904); for recent references see M. J. Ronteix and A. Marquet, *Tetrahedron Letters*, 5801 (1966).

SCHEME I



that enol formation destroys optical activity α to the carbonyl group and in fact rates of halogenation of ketones have been shown to be the same as their rates of racemization.[19] The hydrazidic bromide VIII was converted to the hydrazide X, which was also prepared by another route, starting with the same alcohol VI. This second route involved the mild oxidation of the alcohol to the acid IX which was then converted to the acid chloride and treated with 2,4-dinitrophenylhydrazine to give the hydrazide X. The extent of racemization in each of the steps used in the second route has been established by other workers[20] (and is less than 5% in total) and the hydrazide X obtained had the same specific rotation as a sample prepared by the hydrolysis of the hydrazidic bromide. Other experiments[21] involving bromide replacement from VIII by azide ion also support the view that the bromination step has occurred with complete retention of configuration at the α carbon. It had been reported[22] that the ene–hydrazine form could exist in appreciable amounts in polar solvents, whereas Karabatsos and coworkers[3] on the basis of nmr evidence suggested otherwise. Our results are in agreement with Karabatsos' findings since not only did bromination occur without the formation of the ene–hydrazine (VIIb) but also the hydrazidic bromide (VIII) did not lose optical activity after its being maintained in acetic acid solution for 2 hr at 25°.

The rate data for trimethylacetaldehyde DNP (XI), which cannot form an ene–hydrazine tautomer, are also readily correlated by the line used for all the other alkylidene DNPs (Figure 1); moreover bromination of this DNP also gives a hydrazidic bromide XII (eq 3).

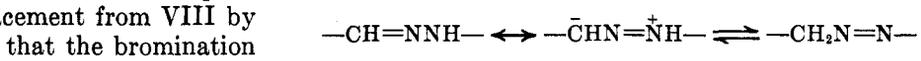


(3)

Also the fact that hydrazidic bromides are the products formed by bromination of alkylidene DNPs rather than α-bromoalkylidene DNPs (which would be formed on bromination of the ene–hydrazines) supports the observation above that ene–hydrazine formation is not the rate-determining step in the bromination of alkylidene DNPs (*i.e.* the slow hydrazone → hydrazone′ conversion).

The bromination of some ketone DNPs was also briefly studied. On bromination these cannot form hydrazidic bromides (except by loss of an alkyl group) and α-bromo ketone DNPs have been reported[23a] as the products from the bromination of some ketone DNPs. The kinetics of the bromination reaction reflect this difference, and are consistent with rate-determining ene–hydrazine formation in this case. The bromination of acetone and of benzyl methyl ketone DNPs were zero order in bromine and their N-MeDNPs were brominated about twice as rapidly as the unmethylated analogs, as expected since the inductive effect of a methyl group should stabilize ene–hydrazine form[23] (by analogy with the observed effects in enol formation[24]) (see Table III); alkylidene N-MeDNPs on the other hand are brominated far less rapidly (Table III) than the DNPs (in both of these cases the products are hydrazidic bromides).

Although tautomerism of hydrazones to azoalkanes might also, in theory, occur, only the opposite reaction is observed, the hydrazone being thermodynamically the more stable.[3c] The saturated carbon of the azoalkane would be less nucleophilic and would not



be expected to react rapidly with bromine[25] (to explain the observed kinetics the azoalkane would have to react about 100 times more rapidly than the hydrazone with bromine). Moreover no evidence for rate-determining azoalkane formation was observed in the bromination of arylidene arylhydrazones[5a] (where such tautomerism is also in theory possible).

N,N-Disubstituted hydrazones have been widely reported to fail to react with electrophiles such as diazonium ion,[26] lead tetraacetate,[27] halogen,[28] nitroso bisulfate,[29] and α-carbonylazo compounds[30] and if examples of simultaneous oxidative cleavage of N-alkyl groups[31] are excluded then there have been no reports of C-substituted products being obtained from such hydrazones (although in almost every case an attempt was made to isolate such a product). The

(19) C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, 772 (1934).

(20) P. A. S. Smith, "Molecular Rearrangements," P. deMayo, Ed. John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 8.

(21) A. F. Hegarty, J. B. Aylward, and F. L. Scott, *Tetrahedron Letters*, 1259 (1967).

(22) A. E. Arbuzov and Y. P. Kitaev, *Dokl. Akad. Nauk SSSR*, 113, 577 (1959); Y. P. Kitaev and T. K. Troepol'skaya, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 454, 463 (1963); Y. P. Kitaev and A. E. Arbuzov, *ibid.*, 1405 (1960); 1037 (1957).

(23) Results from preliminary experiments using a variety of ketone DNPs indicate that substituent effects parallel those for the bromination of substituted acetones, although the DNPs are brominated approximately 10^3 times more rapidly than the parent ketone.

(24) A. Fischer, J. Packer, and J. Vaughan, *J. Chem. Soc.*, 3318 (1962).

(25) J. H. Collins and H. H. Jaffé, *J. Am. Chem. Soc.*, **84**, 4708 (1962).

(26) H. Hauptmann and A. C. Perisse, *Experientia*, **10**, 60 (1954); *Ber.*, **89**, 1081 (1956).

(27) D. C. Iffland, R. Salisbury, and W. R. Schaffer, *J. Am. Chem. Soc.*, **83**, 747 (1961); D. C. Iffland and T. M. Davis, *ibid.*, **85**, 2182 (1963).

(28) J. M. Burgess and M. S. Gibson, *Tetrahedron*, **18**, 1001 (1962); D. B. Sharp, *J. Am. Chem. Soc.*, **71**, 1106 (1949).

(29) H. J. Teuber and K. H. Dietz, *Angew. Chem. Intern. Ed. Engl.*, **5**, 1049 (1966).

(30) E. Fahr and H. D. Rupp, *ibid.*, **3**, 693 (1964); L. Pentimalli and S. Bozzini, *Ann. Chim.* (Rome), **55**, 441 (1965).

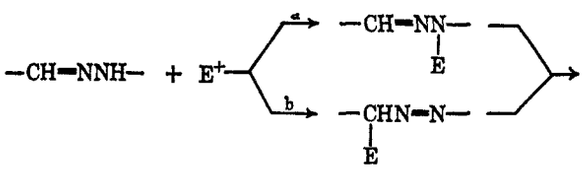
(31) D. C. Iffland and E. Cerda, *J. Org. Chem.*, **28**, 2769 (1963).

TABLE IV
HYDRAZIDIC BROMIDES, $RCBr{=}NNHC_6H_3(NO_2)_2$

R	Mp, °C	Calcd, % C	H	Br	N	Formula	Found, % C	H	Br	N	Yield, %
CH_3	148–150	31.71	2.33	26.37	18.49	$C_8H_7BrN_4O_4$	31.76	2.27	26.83	18.38	84
C_2H_5	114–115	34.08	2.84	25.20	17.67	$C_9H_9BrN_4O_4$	33.99	2.80	25.96	17.75	60
$CH(CH_3)_2$	117–118	36.27	3.35	24.14	16.92	$C_{10}H_{11}BrN_4O_4$	36.13	3.38	24.00	16.84	90
$CHCH_3(C_2H_5)$	103	38.27	3.80	23.15	16.24	$C_{11}H_{13}BrN_4O_4$	38.61	3.84	23.25	16.11	82
$C(CH_3)_3$	155–156	38.27	3.80	23.15	16.24	$C_{11}H_{13}BrN_4O_4$	38.40	3.40	23.38	16.24	83
CH_2Cl	145	28.46	1.80	34.19[a]	16.63	$C_8H_6BrClN_4O_4$	28.77	2.07	34.35[a]	16.32	81
$CHCl_2$	141–142	25.82	1.35	40.54[a]	15.06	$C_8H_5BrCl_2N_4O_4$	25.96	1.32	41.06[a]	15.28	75
CCl_3	158–159	23.64	0.99	45.83[a]	13.80	$C_8H_4BrCl_3N_4O_4$	23.46	0.90	46.63[a]	13.33	80

[a] Total halogen.

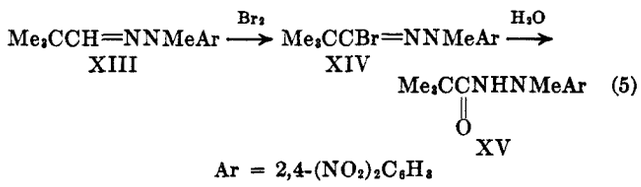
mechanism for electrophilic substitution reactions of hydrazones originally proposed (principally by Busch and his coworkers[32]) involved prior attack by the electrophile at the amino nitrogen of the hydrazone (path a, eq 4), followed by rearrangement from nitro-



(4)

gen to carbon. The two-step mechanism interprets the lack of reactivity of N,N-disubstituted hydrazones as due to the lack of an NH proton. Recently, as a result of kinetic studies and the isolation of some azomethane intermediates,[5,33] we have proposed that electrophilic attack can occur directly at the methine carbon of the hydrazone (pathway b), this being followed by an azohydrazone tautomerism. Reaction with N,N-disubstituted hydrazones could then occur by this pathway b if a sufficiently reactive electrophilic agent was used to overcome the greater energy involved in the loss of the C–H (rather than N–H) proton.

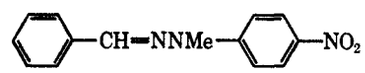
We have found (Table III) that the bromination of alkylidene N-MeDNPs does, in fact, occur though at a reduced rate compared to the unmethylated compounds. These bromination reactions were again zero order in bromine and first order in hydrazone. For one of these hydrazones we also isolated a brominated product. When trimethylacetaldehyde N-MeDNP (XIII) was treated in glacial acetic acid (3 ml/g) with an equimolar quantity of bromine, the hydrazidic bromide XIV precipitated after 40 min, mp 108° (eq 5). This compound was hydrolyzed even



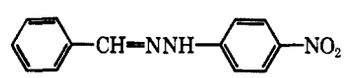
(5)

more readily than the corresponding N-monosubstituted hydrazidic bromide (giving the hydrazide XV)[34] and in fact the hydrazide XV was the only product isolated if excess bromine, or a longer reaction time was used in the reactions of XIII with Br_2. So far only the corresponding hydrazide has been isolated from the bromination of acetaldehyde N-MeDNP; presumably the analogous hydrazidic bromide is also formed but reacts rapidly with the solvent.

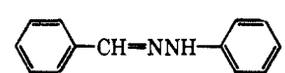
Other N,N-disubstituted hydrazones behave similarly. Thus benzylidene N-methyl-N-*p*-nitrophenylhydrazone (XVI) is also brominated slowly ($k = 3.8 \times 10^{-5}$ sec^{-1}) and the reaction is also zero order in bromine[35] (whereas the bromination of the N–H analog XVII is a rapid second-order reaction).



XVI



XVII



XVIII

The similarity in kinetic behavior between N,N-disubstituted hydrazones and alkylidene DNPs suggests that both groups of compounds react by a similar mechanism. DNPs differ from other N-monosubstituted hydrazones in that the amino hydrogen is tightly hydrogen-bonded to the *o*-nitro group.[3] That it is this factor which is vital in determining the kinetic pattern of these compounds was shown by the facts that (a) the bromination of benzylidene *o*-nitrophenylhydrazone (XVIII) (in contrast to the pattern in the arylidene *p*-nitrophenylhydrazones) is zero order in bromine (with $k_1 = 1.6 \times 10^{-4}$ sec^{-1}) and (b) the bromination of other alkylidene hydrazones, for example, alkylidene, *p*-nitrophenylhydrazones, is similar to the bromination of the arylidene cases (*e.g.*, XVII) in that the reaction is first order each in bromine and the hydrazone. Both N,N-disubstituted hydrazones and *o*-nitrohydrazones react with bromine with loss of a C–H (SE2 mechanism) rather than an N–H (SE2′ mechanism) proton. Both of these reaction mechanisms would have their own steric requirements. From an examination of molecular models, it is apparent that there is little steric hindrance to the formation of an azoalkane (SE2′ mechanism) in either the *syn* or *anti* hydrazone isomers so that bromine presumably reacts rapidly with the isomer (*syn*)

(32) M. Busch and R. Schmidt, *Ber.*, **63**, 1950 (1930); M. Busch and H. Pfeiffer, *ibid.*, **59**, 1162 (1926); M. Busch and H. Kunder, *ibid.*, **49**, 317 (1916); M. Busch, H. Müller, and E. Schwarz, *ibid.*, **56**, 1600 (1923).

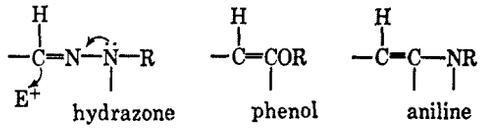
(33) A. F. Hegarty and F. L. Scott, *Chem. Commun.*, 622 (1966); *J. Org. Chem.*, **32**, 1957 (1967).

(34) F. L. Scott and J. B. Aylward, *Tetrahedron Letters*, 841 (1965).

(35) Results obtained (A. F. Hegarty, F. A. Groeger, to be published) for substituent variation in the hydrazone XVI also parallel those for the bromination of alkylidene DNPs; *e.g.*, the rate of bromination of XVI was independent of the nature of *meta* or *para* substituents in the arylidene ring, while *ortho* substituents in this ring have a simple steric effect (correlated by the Taft equation).

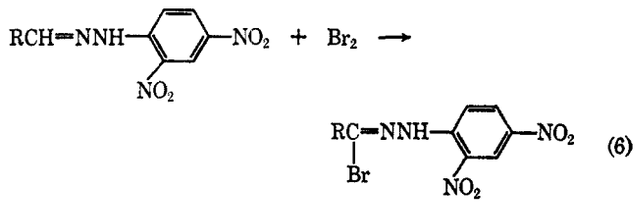
present in excess. But in those compounds which react by an SE2 mechanism (either because the amino nitrogen of the hydrazone is disubstituted or there is an o-nitro group present) there is apparently a large difference in the accessibility of the methine carbon and the steric requirements of the transition state (since the N-alkyl or N–H is retained) in the reactions with both hydrazone isomers. This difference in reactivity is sufficiently large in this SE2 reaction so that the relatively slow hydrazone *syn* to *anti* conversion becomes rate determining.

This duality of mechanism SE2′ and SE2 has also been described for phenols (and anisoles)[36,37] and it is likely that a similar classification could be applied to anilines. The SE2 process had been well known for phenols and the SE2′ was established recently[36] by an isotopic effect in the bromination of O-deuteriophenol.

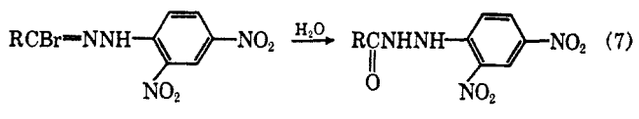


R = CH_3, SE2
R = H, SE2′

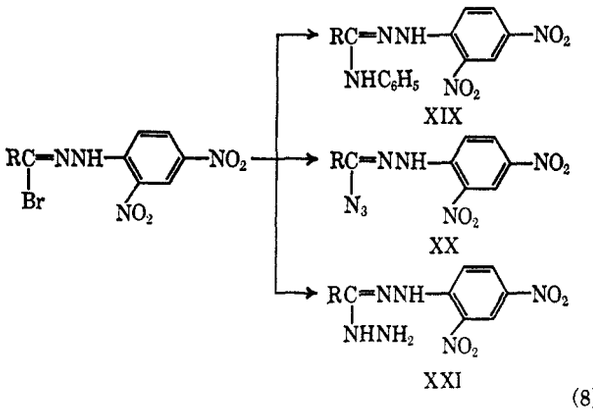
Alkylhydrazidic Bromides.—A key factor in our interpretation of the mechanism of bromination of alkylidene DNPs is the nature of the products. As stated previously, these were formed by exclusive methine substitution and represented the novel compounds, the alkylhydrazidic bromides. The hydrazidic bromides were formed in best yields when the hydrazone was stirred as a slurry in acetic acid and a large excess (usually fivefold) of bromine was added all at once (eq 6). The method was successful for the



preparation of hydrazidic bromides with R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $CHCH_3(C_2H_5)$, $C(CH_3)_3$, CH_2Cl, $CHCl_2$, and CCl_3 (see Table IV for melting point and analytical data). On hydrolysis, in 50% aqueous acetone at reflux, the hydrazidic bromides were converted smoothly to alkylhydrazides (eq 7), thus



confirming that the substrates were, in fact, hydrazidic bromides. The hydrazides were also prepared unambiguously by coupling the acid chloride with 2,4-dinitrophenylhydrazine, or in some cases by the direct reaction of the acid with hydrazine. The reactions of alkylhydrazidic bromides parallel those of the aryl analogs, replacement of the halogen occurring even more readily. Thus the bromine was replaced by aniline to give an amidrazone XIX, by azide ion to give a hydrazidic azide XX, and by hydrazine to give a hydrazidine XXI (eq 8).



On hydrolysis the di- and trichloromethylhydrazidic bromides underwent extensive decomposition; this is not surprising since they should be highly reactive. Chattaway and coworkers,[38] with a view to preparing the corresponding hydrazidic bromides, made many attempts to prepare the starting hydrazones and failed. More recently[39] use of concentrated hydrochloric acid as a reaction medium made these hydrazones available. We have found that once formed these chlorohydrazones may be brominated smoothly in acetic acid.

Experimental Section

Melting points are corrected and were obtained on an Electrothermal capillary melting point apparatus. Elemental analyses were supplied by Pascher and Pascher, Bonn, Germany. Ultraviolet spectra were measured in 95% ethanol solution, using a Perkin-Elmer 137 uv spectrophotometer. Nmr spectra were recorded on a Varian HA-100 spectrometer with tetramethylsilane as internal reference and deuteriochloroform as solvent. Optical rotation measurements were made using a Perkin-Elmer Model 141 polarimeter.

Materials.—Potassium bromide, potassium nitrate, and all inorganic materials used were AnalaR grade. The reaction solutions were prepared from water which had been triply distilled from alkaline potassium permanganate and acetic acid which had been distilled from chromium trioxide (bp 117–118°). The 70% acetic acid used as solvent for the kinetic experiments was prepared by mixing 70 volumes of acetic acid with 30 volumes of water at 20°. The aldehydes and ketones used were commercially available. The liquid materials were distilled and the solids recrystallized from aqueous ethanol before use. 2,4-Dinitrophenylhydrazine (Reagent grade) was once recrystallized from ethanol.

Substrates.—The 2,4-dinitrophenylhydrazones (DNPs) of aliphatic aldehydes and ketones were prepared in a rigorously similar manner by adding the carbonyl compound (7×10^{-2} mole) in methanol (10 ml) to 2,4-dinitrophenylhydrazine (10 g) dissolved in methanol (400 ml) and concentrated sulfuric acid (10 ml). The DNPs precipitated immediately and were collected after 1 hr and thoroughly washed clear of the catalyzing acid (with water). Each DNP was then crystallized three times from aqueous ethanol, the crystallization being carried out as rapidly as possible to minimize, as far as possible, the equilibration of *syn* and *anti* isomers; the generally sharp melting points obtained indicate the presence of only one (*syn*) isomer.[38a] The following aldehyde DNPs ($RCH{=}NNHC_6H_3(NO_2)_2$) were used: R = CH_3, mp 161–162° (lit.[40] mp 168, 160,

(36) P. B. D. de la Mare and O. M. H. El Dusouqui, *J. Chem. Soc., Sect. B*, 251 (1967).

(37) C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed, *ibid.*, 2628 (1950).

(38) F. D. Chattaway and C. H. Farinholt, *ibid.*, 94 (1930); F. D. Chattaway and A. Adair, *ibid.*, 2850 (1927); 1488 (1938); F. D. Chattaway and T. E. W. Browne, *ibid.*, 1089 (1931).

(39) A. Ross and R. N. Ring, *J. Org. Chem.*, **26**, 579 (1961).

(40) C. D. Hodgemann, *et al.*, "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, pp 68–80.

TABLE V

N-METHYL-N-(2,4-DINITROPHENYL)HYDRAZONES, $RC(R')=NN(CH_3)C_6H_3(NO_2)_2$

R	R'	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Formula	Found, % C	Found, % H	Found, % N
$CH(CH_3)_2$	H	105–106	49.63	5.30	21.06	$C_{11}H_{14}N_4O_4$ (a)	49.39	5.39	21.32
$C(CH_3)_3$	H	105	51.46	6.86	20.01	$C_{12}H_{16}N_4O_4$ (b)	51.27	6.87	19.86
CH_3	CH_3	135–137	47.65	4.79	22.20	$C_{10}H_{12}N_4O_4$ (c)	47.61	4.95	21.56
$CH_2C_6H_5$	CH_3	164–165	58.59	4.92	17.08	$C_{16}H_{16}N_4O_4$ (d)	58.94	5.23	16.62

TABLE VI

N-(2,4-DINITROPHENYL)ALKYLHYDRAZIDES, $RCONHNHC_6H_3(NO_2)_2$

R[a]	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Formula	Found, % C	Found, % H	Found, % N
C_2H_5	184	42.52	4.06	22.05	$C_9H_{10}N_4O_5$ (a)	42.37	4.20	22.30
$CH(CH_3)_2$	205–206	44.78	4.51	20.89	$C_{10}H_{12}N_4O_5$ (b)	44.57	4.43	20.94
$CH(C_2H_5)CH_3$	178	46.80	4.98	19.85	$C_{11}H_{14}N_4O_5$ (c)	46.29	5.20	20.10
$C(CH_3)_3$	185–186	46.80	4.98	19.85	$C_{11}H_{14}N_4O_5$ (d)	46.86	4.84	19.71

[a] With R = CH_3, mp 199° (lit.[b] 199.5°) and, with R = CH_2Cl, mp 200–201° (lit.[c] 199–200°) were obtained. [b] P. A. Abramovitch and K. Schofield, *J. Chem. Soc.*, 2326 (1935). [c] J. Cerezo and E. Olay, *Anales. Soc. Españ. Fis. Quim.*, **32**, 1090 (1934).

149°) (for a discussion of these and related discrepancies below see Karabatsos[3]); CH_3CH_2, 151–152° (lit.[40] 148°); $(CH_3)_2CH$, 182° (lit.[40] 182, 187°); $CH_3(C_2H_5)CH$, 130° (lit.[40] 121°); $(CH_3)_3C$, 210° (lit.[40] 210°); $C_6H_5CH_2$, 120–121° (lit.[40] 121°). When prepared under these conditions, the chloroaldehyde DNPs lost hydrochloric acid with the formation of compounds of the type $RCH{=}CHN{=}NC_6H_3(NO_2)_2$.[38] These DNPs (see below) were prepared by the following general method. 2,4-Dinitrophenylhydrazine (5.0 g) was stirred vigorously in 12 *N* hydrochloric acid (300 ml) at 40°. The aldehyde (0.1 mole) was added dropwise over a period of 1 hr, the temperature being maintained at 40° throughout. On cooling the mixture in ice the aldehyde DNP was collected (in approximately theoretical yield) on a sintered glass funnel and washed thoroughly clear of hydrochloric acid. The DNPs were then twice crystallized from carbon tetrachloride: R = $ClCH_2$, mp 156–158° (lit.[39] 158.5–160.5°); Cl_2CH, 137–139° (lit.[39] 146°); Cl_3C, 147–149° (lit.[39] 152–158°).

N-Methyl-N-2,4-dinitrophenylhydrazones.—The carbonyl compound (3×10^{-2} mole), dissolved in ethanol (5 ml), was added to N-methyl-N-2,4-dinitrophenylhydrazine (5 g) in ethanol (20 ml) and concentrated sulfuric acid (4 ml). The hydrazine had been prepared, mp 142°, from the reaction of 1-chloro-2,4-dinitrobenzene and methylhydrazine in ethanol. The N-MeDNPs were precipitated by cooling the solution in ice (after heating the solution at 60° for 10 min), and recrystallized to constant melting point (see Table V).

Benzylidene N-Methyl-N-*p*-nitrophenylhydrazone.—An attempt to prepare this compound by the method of Kenyon and Hauser[41] in liquid ammonia–sodamide failed; the deep purple color characteristic of the hydrazone anion formed immediately on dissolution in ammonia but was not discharged when methyl iodide was added. The methylation was, however, achieved using sodium hydroxide solution. Benzylidene *p*-nitrophenylhydrazone (2.41 g) was added to 3 *N* sodium hydroxide (6.6 ml) and water (20 ml) and on the addition of acetone (20 ml), the deep purple salt of the hydrazone was formed. Methyl iodide (2.84 g) was added and, when the solution had stood at room temperature for 3 days, the N-methylhydrazone (2.1 g, 82%) precipitated, mp 136–137° (lit.[42] mp 137°) on crystallization from ethanol.

Anal. Calcd for $C_{14}H_{13}N_3O_2$: C, 65.92; H, 5.13; N, 16.47. Found: C, 66.07; H, 5.17; N, 16.64.

1-(2′,4′-Dinitrophenyl)-2-pyrazoline.—Hydrazine hydrate (5.0 g) was dissolved in ethanol (5 ml) and cooled in an ice–salt bath and rapidly stirred while freshly distilled acrolein (5.6 g) was added dropwise (over a period of 30 min). The solution was gently refluxed for 2 hr and 2-pyrazoline, bp 136–144° (760 mm), was distilled off (3.1 g, 44%). On redistillation the fraction with bp 142–144° was retained (lit.[43] bp 144°). 2-Pyrazoline (1.0 g) dissolved in ethanol (5 ml) was added to 1-chloro-2,4-dinitrobenzene (2.5 g) in ethanol (20 ml) at 60° and maintained at that temperature for 30 min. On cooling, 1-(2′,4′-dinitrophenyl)-2-pyrazoline separated, mp 114–115° on recrystallization from aqueous ethanol. This is rather higher than the lit.[45] mp 106° but spectral and analytical data are consistent with this structure, as is its conversion to the known 3-bromo derivative.

Anal. Calcd for $C_9H_8N_4O_4$: C, 45.76; H, 3.41; N, 23.74. Found: C, 45.72; H, 3.45; N, 23.86.

Bromine (0.08 ml) was added to 1-(2′,4′-dinitrophenyl)-2-pyrazoline (300 mg), dissolved in 10 ml of dry chloroform and the solution was refluxed for 2 hr. The solution was then concentrated to 5 ml when 3-bromo-1-(2′,4′-dinitrophenyl)-2-pyrazoline, mp 166–168° on recrystallization from benzene–petroleum ether (bp 40–60°), lit.[44] mp 168–169°.

Kinetic Studies.—The kinetics of bromination of DNPs were studied by an electrometric method in which low bromine concentrations were monitored by recording the diffusion current of bromine at a rotated platinum electrode. In the solvent used, 70% acetic acid containing 0.1 *M* potassium bromide, the most suitable polarizing voltage was +0.2 v with respect to the silver–silver chloride reference electrode. This polarizing voltage was supplied by a Metrohm Polarecord E261-R which also, as a sensitive galvanometer, plotted the decay in the bromine diffusion current when the DNP was introduced to the reaction cell. Bromine, instead of being added in a concentrated form from a standard solution, as previously described,[5] was electrogenerated in small precisely known amounts from the potassium bromide solution using a constant current (usually 1 ma). A Metrohm E211 coulometer supplied this current and was used with a platinum gauze (5 cm^2) generating electrode as anode and a silver gauze (20 cm^2) auxiliary electrode. The silver cathode was dipped in a saturated solution of potassium nitrate and was separated from the reaction solution by a sintered glass disk and an agar plug. The deflection of the recorder pen in the indicator circuit was shown to be proportional to the electrolysis time used to generate bromine at various bromide ion concentrations, *i.e.*, the indicator circuit measures the total analytical concentration of bromine, $Br_2 + Br_3^-$, and is independent of the relative amounts of these two species present.

All the kinetic experiments were at 20°. The DNPs were not sufficiently soluble in 70% acetic acid to be added in concentrated form to the reaction cell. They were therefore made up, usually in 10^{-2} *M*, solution in glacial acetic acid, and 1.0 ml of this solution was added (using a calibrated syringe) to 20 ml of the reaction in the cell to start the reaction. The 20-ml reaction solution in the cell had to accommodate 1.0 ml of glacial acetic acid. Thus 68.5% acetic acid–31.5% water containing 12.4971 g of potassium bromide per liter gave a final composition of 70% acetic acid containing 0.1 *M* potassium bromide when 20 ml was added to 1.0 ml of glacial acetic acid.

(41) W. D. Kenyon and C. R. Hauser, *J. Org. Chem.*, **30**, 292 (1965).
(42) L. Maaskant, *Rec. Trav. Chim.*, **56**, 211 (1937).
(43) M. Mousseron, R. Jacquier, and J. Brun, *Compt. Rend.*, **247**, 617 (1958).
(44) J. Elguero and R. Jacquier, *Bull. Soc. Chim. France*, 610 (1966).

In a typical kinetic experiment 20 ml of the reaction solution was pipetted into the water-jacketed reaction cell and, after 15 min, the electrolysis was commenced to generate the desired quantity of bromine. When the electrolysis was complete the indicator circuit recorder plotted a diffusion current proportional to the amount of bromine generated. With carefully purified solvents, reaction of bromine with solvent even at the low concentrations used was negligible and could be ignored. The DNP, dissolved in 1.0 ml glacial acetic acid, was then introduced into the cell (using a calibrated syringe) and the recorder plotted a bromine concentration (in arbitrary units) *vs.* a time curve. Since the DNP was usually in a large excess and the reactions were zero order in bromine, these plots were rectilinear. From the slopes of these lines and the known concentration of the DNP used, the rate constants, k_1 in sec^{-1}, were calculated.

Product Analysis. N-(2,4-Dinitrophenyl)-C-alkylhydrazidic Bromides.—The alkylidene DNP (10^{-2} mole) was suspended in glacial acetic acid (8 ml) containing 2% acetic anhydride, and vigorously stirred while bromine (3 ml) in acetic acid (2 ml) was added rapidly. The hydrazone immediately dissolved and the N-(2,4-dinitrophenyl)-C-alkylhydrazidic bromide precipitated, usually in 80–85% yield, after 2–10 min, the time depending mainly on the reactivity of the DNP. The hydrazidic bromides were washed with petroleum ether (bp 40–60°) and crystallized (usually four times) to constant melting point (Table IV). Water was not added to the acetic acid solutions used to crystallize the hydrazidic bromides since these compounds were readily hydrolyzed to alkylhydrazides.

Product Analysis in Kinetic Experiments.—As noted previously in other studies,[5] at the low bromine concentrations used, only a small amount (~1 mg) of the substrate was brominated in a kinetic experiment. It was therefore difficult (and this problem was more acute when the DNP was in a large excess) to separate the small amount of product formed by, *e.g.*, fractional crystallization (to confirm that the brominated product was the same as obtained when the experiment was carried out on a large scale). As before,[5a] however, this separation was readily achieved using thin layer chromatography. Thus, *e.g.*, acetaldehyde DNP (R_f = 0.46) could be separated from the corresponding hydrazidic bromide (R_f = 0.71) on silica gel G (Merck) using benzene as mobile phase. Under the conditions used to study the kinetics therefore the hydrazidic bromides (Table IV) were shown to be the product formed from the corresponding DNPs, even when the DNPs were in a 50-fold excess (relative to bromine). α-Bromoacetone DNP has been shown[2a] to be the product obtained by the bromination of acetone DNP in 90% acetic acid. We confirmed this using the thin layer technique when 70% acetic acid was used as solvent but in addition a small amount of an unidentified material was also obtained in the bromination reactions in this solvent.

N-(2,4-Dinitrophenyl)-C-alkylhydrazides.—The N-(2,4-dinitrophenyl)-C-alkylhydrazidic bromide (2×10^{-3} mole) was dissolved in a 1:1 mixture of acetone–water (40 ml) and extracted with three 20-ml portions of ether. On evaporation of the dried ethereal extracts the hydrazides were obtained in 60—90% yield. They were crystallized to constant melting point from aqueous ethanol (Table VI). Titration of the aqueous portion from the reaction solution by Volhard's method showed that the theoretical amount (±3%) of bromide ion had been liberated in all cases. The alkylhydrazides were also unambiguously prepared by refluxing 2,4-dinitrophenylhydrazine (2 g) with an excess of the aliphatic acid (20 ml) for 18 hr. On cooling the hydrazides (from acetic, propionic, isobutyric, and chloroacetic acids) precipitated and after two crystallizations from aqueous ethanol were found to be identical (mixture melting point and infrared spectra) with those prepared above. The other hydrazides were prepared by mixing equimolar quantities of the acid chlorides and 2,4-dinitrophenylhydrazine in pyridine. Other replacement reactions (described for one compound below) confirmed the hydrazidic bromide structure.

N-(2,4-Dinitrophenyl)-N′-phenyl-C-(2′-butyl)amidrazone.—N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazidic bromide (100 mg) was treated with redistilled aniline (0.1 ml). Immediately a deep red solution was obtained which was stirred at 40° for 5 min. On cooling the mixture was poured into ether (10 ml) and extracted twice with 5 ml of water. The deep red ethereal layer was dried (sodium sulfate) and evaporated to give a residue with a strong odor of aniline. Ethanol (20 ml) was added and the mixture heated until a solution was obtained. The solution was filtered and on cooling the amidrazone (102 mg, 97%) separated, mp 117–118°. On crystallization from aqueous ethanol the melting point was raised to 125°.

Anal. Calcd for $C_{17}H_{19}N_5O_4$: C, 57.19; H, 5.36; N, 19.62. Found: C, 56.92; H, 5.26; N, 19.60.

N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazidic Azide.—N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazidic bromide (100 mg) was added to 80% dioxane–water and heated to 25° when a clear solution was obtained. To this was added sodium azide (37.8 mg) dissolved in 2 ml of the same solvent. The hydrazidic azide precipitated rapidly, mp 140° (80 mg, 90%). On crystallization from water–acetone the hydrazidic azide had mp 140–141°; the infrared spectrum of this compound showed the strong characteristic azide absorption at 4.66 μ.

Anal. Calcd for $C_{11}H_{13}N_7O_4$: C, 43.03; H, 4.27; N, 31.93. Found: C, 43.29; H, 4.49; N, 32.35.

N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazidic bromide (300 mg) was stirred as a slurry with 5 ml of 95% ethanol at room temperature and hydrazine hydrate (0.3 ml) was added dropwise. The solution became deep red and a brown-red solid precipitated. This was collected after a further 15 min (220 mg, 84%), mp 172–174°. Recrystallization (three times) from aqueous ethanol gave the hydrazidine, mp 180°.

Anal. Calcd for $C_{11}H_{16}N_6O_4$: C, 44.63; H, 5.45; N, 28.39. Found: C, 44.90; H, 5.64; N, 28.25.

This hydrazidine was characterized as its benzal derivative by the reaction of equimolar quantities of benzaldehyde and the hydrazidine in ethanol. The benzal derivative had mp 175°.

Anal. Calcd for $C_{18}H_{20}N_6O_4$: C, 56.30; H, 5.25; N, 21.89. Found: C, 56.74; H, 5.16; N, 21.56.

Optically Active N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazidic Bromide.—D-(−)-2-Methyl-1-butanol ($[\alpha]_{578}^{25} = -5.80°$ (neat), 15 g) was rapidly stirred while being heated in a 250-ml flask with a Claisen head and a condenser set downward for distillation. To this was added, over 20 min, potassium chromate (19 g) in water (100 ml) and concentrated sulfuric acid (14 ml), the solution being maintained at 72–73° (200 mm). The aldehyde was removed by azeotropic distillation at this temperature and after careful separation from the water was dried (sodium sulfate). Distillation then yielded D-(+)-2-methylbutyraldehyde (11.2 g, 75%), bp 90–92° (lit.[45] 91.5–92°), sufficiently pure for hydrazone formation. The DNP of this aldehyde was prepared in the usual way (see above), the time in contact with the acid catalyst being kept to a minimum. The D-(+)-2-Methylbutyraldehyde DNP had specific rotation $[\alpha]_{578}^{25}$ +32.0° (*c* 1.0, acetone) (lit.[46] $[\alpha]_{578}^{25}$ +32.1°). The optically active DNP (1.0 g) was rapidly stirred with acetic acid (3 ml) and bromine (1.0 ml) in acetic acid (1.0 ml) was added. The hydrazidic bromide formed was collected after 3 min, mp 99–100° (for analytical data see Table IV). The N-(2,4-dinitrophenyl)-C-(2′-butyl)hydrazidic bromide had a specific rotation $[\alpha]_{578}^{25}$ +21.0° (*c* 1.0, acetone) and $[\alpha]_{578}^{25}$ +18.0° (*c* 1.0, acetic acid) and this latter value had not changed when the hydrazidic bromide had stood in acetic acid solution for 2 hr at 25°.

N-(2,4-Dinitrophenyl)-C-(2′-butyl)hydrazide. A.—Optically active N-(2,4-dinitrophenyl)-C-(2′-butyl)hydrazidic bromide (200 mg) was heated at 70° for 2 hr in 1:1 acetone–water (40 ml). On cooling, the addition of water (20 ml) precipitated the hydrazide, mp 176–178° (in 82% yield) with $[\alpha]_{578}^{25}$ +26.7° (*c* 0.8, acetone).

B.—D-(−)-2-Methyl-1-butanol (20 g) was added dropwise (10 min) to a stirred solution of potassium permanganate (52 g) and potassium hydroxide (6 g) in 1 l. of water at room temperature. The mixture was stirred for 40 min and extracted with two 50-ml portions of ether and the aqueous layer acidified with hydrochloric acid. Extraction with chloroform (150 ml) removed the optically active acid. The chloroform was washed with two 50-ml portions of water and dried (sodium sulfate). The chloroform was removed by distillation and 2-methylbutyric acid was obtained (10.65 g, 47.5%) by fractionation through a 10-in. column, bp 175–177° (lit.[47] bp 175–177°). The acid (9 g) was added over a period of 40 min to gently refluxing thionyl chloride (11.6 g), and the solution was refluxed for a further 2 hr when D-(+)-2-methylbutyryl chloride (8.88 g,

(45) L. Lardicci and R. Rossi, *Atti Soc. Toscana Sci. Nat. Pisa, Proc. Verbali Mem. Ser. A*, **68**, 23 (1962).

(46) E. J. Badin and E. Pascu, *J. Am. Chem. Soc.*, **67**, 1352 (1945).

(47) K. Sax and W. Bergmann, *ibid.*, **77**, 1910 (1955).

84%) was obtained, bp 116–117° (lit.[48] 114–116°). The acid chloride (1.0 ml) was added to 2,4-dinitrophenylhydrazine (1.0 g) in pyridine (30 ml) and the solution was heated at 100° for 5 min. On cooling the solution was poured on ice chips (50 g) and the hydrazide was precipitated, mp 165–170°. On crystallization from aqueous ethanol the same hydrazide was obtained as by method A above, mp 176–177°, with $[\alpha]_{578}^{25}$ +26.6° (c 1.0, acetone).

Bromination of Trimethylacetaldehyde N-Methyl-N-2,4-dinitrophenylhydrazone. A.—The hydrazone (1.0 g) was suspended as a slurry with acetic acid (3.0 ml) containing acetic anhydride (10%) and the mixture was rapidly stirred while bromine (0.2 ml) was added (over a period of 30 sec). The hydrazone dissolved and after 30–40 min the N-methyl-N-(2,4-dinitrophenyl)-C-(*t*-butyl)hydrazidic bromide precipitated, mp 103° (910 mg, 70%). Crystallization from acetic acid raised the melting point of the hydrazidic bromide to 108°.

Anal. Calcd for $C_{12}H_{15}BrN_4O_4$: C, 40.15; H, 4.21; Br, 22.26; N, 15.61. Found: C, 40.37; H, 4.18; Br, 21.93; N, 15.65.

The nmr spectrum is also consistent with the hydrazidic bromide structure. The peak at τ 3.09 ppm assigned to the methine proton, present in the starting hydrazone, is absent in the hydrazidic bromide.

B. With Excess Bromine.—The hydrazone (1.0 g) was stirred with glacial acetic acid (4.0 ml) and bromine (1.0 ml) in acetic acid (1.0 ml) was added. When the solution had stirred for 24 hr, a light yellow solid had precipitated, mp 168–170° (760 mg). After two recrystallizations from aqueous ethanol the melting point was raised to 176° and the compound was shown to be N-methyl-N-(2,4-dinitrophenyl)-C-(*t*-butyl)-hydrazide which was also unambiguously prepared by the reaction of equimolar quantities of trimethyl acetyl chloride and N-methyl-N-2,4-dinitrophenylhydrazine in pyridine.

Anal. Calcd for $C_{12}H_{16}N_4O_5$: C, 48.64; H, 5.45; N, 18.93. Found: C, 48.76; H, 4.90; N, 19.60.

(48) K. B. Wiberg and T. W. Hutton, *J. Am. Chem. Soc.*, **78**, 1640 (1956).

Registry No.—IIa, 15009-34-4; IIb, 14947-23-0; IIc, 14947-24-1; IId, 14947-25-2; IIe, 14947-26-3; IIf, 14947-27-4; IIg, 14947-28-5; IIh, 14947-29-6; IV-(Ar-2,4-$(NO_2)_2C_6H_3$), 5920-44-5; Table V, a, 15009-36-6; Table V, b, 14947-30-9; Table V, c, 14947-31-0; Table V, d, 14947-32-1; Table VI, a, 6561-63-3; Table VI, b, 7461-93-0; Table VI, c, 14947-35-4; Table VI, d, 14947-36-5; N-(2,4-dinitrophenyl)-N′-phenyl-C-(2′-butyl)amidiazone, 14947-37-6; N-(2,4-dinitrophenyl)-C-(2′-butyl)hydrazidic azides, 14947-38-7; N-(2,4-dinitrophenyl)-C-(2′-butyl)hydrazidine, 14947-39-8; N-(2,4-dinitrophenyl)-C-(2′-butyl)hydrazidine benzal derivative, 15077-12-0; N-methyl-N-(2,4-dinitrophenyl)-C-*t*-butyl)hydrazidic bromide, 14947-40-1; N-methyl-N-(2,4-dinitrophenyl)-C-(*t*-butyl)hydrazide, 14947-41-2; benzylidine - N - methyl - N - *p* - nitrophenylhydrazone, 14947-42-3.

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Oxidation of Hydrazones. III. α,β-Unsaturated Monoalkylhydrazones[1,2]

BERNARD T. GILLIS AND MAURICE P. LAMONTAGNE

Chemistry Department, Duquesne University, Pittsburgh, Pennsylvania 15219

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The oxidation of cinnamaldehyde monomethylhydrazone (**1**) with lead tetraacetate in methylene chloride yields N-acetylcinnamic acid methylhydrazide (**2**). When this oxidation is carried out in ether as solvent, acylation occurs to give N-acetylcinnamaldehyde methylhydrazone (**3**). The peracetic acid oxidation of **1** has been found to give the azoxy acetate **4**. The oxidation of isophorone monomethylhydrazone with either lead tetraacetate or peracetic acid has been found to yield an 8:1 ratio of azo acetates **6** and **7**. Also the oxidation of 3-methyl-2-cyclopenten-1-one monomethylhydrazone with either oxidant affords a 2.2:1 ratio of azo acetates **9** and **10**. In contrast, however, oxidation of 2-cyclohexen-1-one monomethylhydrazone with either reagent has been found to yield the azo acetate **12** exclusively.

The oxidation of saturated monoalkylhydrazones with lead tetraacetate or peracetic acid has been investigated by many workers.[3] We wished to add to the research in this area by studying the lead tetraacetate and peracetic acid oxidations of α,β-unsaturated aldehyde and ketone monoalkylhydrazones.

Cinnamaldehyde monomethylhydrazone was prepared by the reaction of cinnamaldehyde and monomethylhydrazine in diethyl ether. The crude product obtained after removal of the solvent was used without any further purification since attempted distillation resulted in extensive cyclization to 1-methyl-2-phenyl-Δ⁴-pyrazoline.[4] The hydrazone was estimated to be about 85% pure by comparison of its ultraviolet maximum and molar absorptivity with that of a pure sample of cinnamaldehyde dimethylhydrazone. Infrared and nmr spectral data also showed the crude hydrazone to be about 85% pure. The yields obtained in the oxidations of this hydrazone were calculated on the basis of 85% purity of the crude hydrazone.

When cinnamaldehyde monomethylhydrazone (**1**) is oxidized with lead tetraacetate in methylene chloride a 44% yield of N-acetylcinnamic acid methylhydrazide (**2**) is obtained. Assignment of this structure is made on the basis of infrared, ultraviolet, and nmr spectral data and microanalysis. On the contrary, when the oxidation is carried out in diethyl ether as solvent, acylation occurs giving rise to N-acetylcinnamaldehyde monomethylhydrazone (**3**).

(1) This investigation was supported by Public Health Service Grant AI-02923 from the National Institute of Allergy and Infectious Diseases.

(2) For the preceding publication in this series, see ref 3e.

(3) (a) D. C. Iffland, L. Salisbury, and W. R. Schafer, *J. Am. Chem. Soc.*, **83**, 747 (1961); (b) W. A. F. Gladstone and R. C. Norman, *J. Chem. Soc.*, 3048, 5177 (1965); (c) F. L. Scott and R. N. Butler, *ibid.*, 1202 (1966); (d) B. T. Gillis and K. F. Schimmel, *J. Org. Chem.*, **27**, 413 (1962); (e) B. T. Gillis and K. F. Schimmel, *ibid.*, **32**, 2865 (1967); (f) J. P. Freeman, *ibid.*, **28**, 2508 (1963).

(4) von K. v. Auwers and P. Heimke, *Ann.*, **458**, 211 (1927).