

The Chlorination of 3,5-Dimethyl-1,2,4-oxadiazole

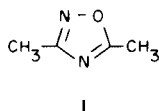
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The chlorination of 3,5-dimethyl-1,2,4-oxadiazole has been studied using both photo and thermal initiation. It has been found that photoinitiation allows reaction at both the 3- and 5-methyl group, the former being preferred by a factor of 3-4 at moderate (up to 75°) temperature. The difference in reactivity is related to a difference in electron availability at the two reaction sites. The thermally initiated chlorination occurs almost exclusively at the 5-methyl group. Overall, 3,5-dimethyl oxadiazole is much less active than toluene or cyclohexane toward chlorination.

3,5-Dimethyl-1,2,4-oxadiazole (3,5-DMO) (I) is uniquely suited to demonstrate the influence of environment, *i.e.*, electron density, on the relative reactivities of its methyl substituents. These effects have been examined by studying the chlorination of 3,5-DMO under a variety of conditions.



The effect of electron-withdrawing groups in reducing the reactivity of carbon-hydrogen bonds toward abstraction in free radical chlorination has been shown kinetically (1,2,3,4) in a number of aromatic systems and has been cited as the reason for the lack of reactivity for carbon-hydrogen bonds *alpha* to the functional groups in aliphatic acids, esters, nitriles, *etc.* (5) in such reactions. The suggestion was made over two decades ago (6) that this diminished reactivity was due to the contribution of polar structures in electrophilic radical attack (7).

The same factors, *i.e.*, electron availability, may also be important in determining the relative reactivities of side chains, *e.g.*, methyl groups, on heterocyclic and aromatic nuclei. This influence is apparent when trimethylisoxazole (8) and trimethylthiazole (9) are caused to react with *N*-bromosuccinimide under radical conditions. In each case, the product is the 4-bromomethyl derivative. A similar affect may be controlling in the reaction of 2-phenyl-4,5-dimethyloxazole with bromide (10). Electron availability is also apparently important in the radical halogenation of xylene isomers and their halogenated derivatives (11).

Discussion.

The remarkably low relative reactivity of 3,5-DMO toward radical chlorination, as demonstrated by competition experiments with cyclohexane or toluene, is clearly indicative of a low relative electron availability at the methyl substituents of 3,5-DMO (12,13).

That both methyls of 3,5-DMO may react by a radical mechanism is demonstrated by the fact that, at moderate temperatures (up to 75°), reaction with chlorine occurs quite slowly or not at all in the dark but readily in the presence of light (Tables I and II). Under radical conditions the 3-methyl group is more reactive than the 5-methyl (Tables I, II and III).

In preliminary experiments with chlorine it was noted that the reactivity of the 5-methyl group increased with temperature, particularly above 75°. On this basis it was predicted that thermally initiated chlorination in the dark might result in almost exclusive 5-methyl chlorination. This was found to be the case for when chlorine was passed into 3,5-DMO at 106° in the dark until essentially all starting material was reacted the product obtained was 88 percent 3-methyl-5-trichloromethyl-1,2,4-oxadiazole (Run 4, Table I).

Irradiation of a reaction at 106° (Run 5, Table I) caused increased reaction at the 3-methyl group but had no remarkable effect on the 5-methyl. It appears that both methyl groups may react by radical mechanisms but at temperatures approximating 100° the 5-methyl also reacts by another, most probably ionic, mechanism. The ionic nature of this mechanism is indicated by the tendency toward polychlorination of the 5-methyl under thermal conditions, *i.e.*, an increase in reactivity is noted with increased chlorination.

TABLE I
Effect of Various Chlorine Sources on the Chlorination of 3,5-DMO

Run Number	3,5-DMO, moles	Chlorine Source, moles	Temp., °C	Initiator, moles	3,5-DMO	3-ClCH ₂ -	5-ClCH ₂ -	3-Cl ₂ CH-	5-Cl ₂ CH-	5-Cl ₃ C-	Time, hours	A ₃ /A ₅ (a)
1	0.4	Cl ₂	48	ISL (b)	60.2	28.0	4.9	3.8	---	0.9	11	---
2	0.4	Cl ₂	46	none	95.9	0.4	2.8	---	0.7	0.2	14	---
3	0.4	Cl ₂	74	none	73.8	1.0	8.2	---	4.9	12.0	16	---
4	0.4	Cl ₂	106	none	9.7	2.1	4.0	---	2.9	81.3	14	---
5	0.4	Cl ₂	106	ISL (b)	0.0	15.1	0.0	9.8	---	34.6	9	---
6	0.05	SO ₂ Cl ₂ (0.01) (c)	40	ISL (b)	70.2	23.5	4.7	1.3	---	---	4	5.4
7	0.1	SO ₂ Cl ₂ (0.05)	35-100	ISL (b)	72.4	16.3	4.4	1.0	2.9	1.0	---	---
8	0.1	SO ₂ Cl ₂ (0.05)	72-106	none	79.2	1.9	5.6	---	6.8	6.4	---	---
9	0.1	SO ₂ Cl ₂ (0.05)	71-106	BP (b) (0.01)	57.6	27.9	7.4	1.9	1.3	1.3	2	---
10	0.05	NCS (b) (0.05)	d	BP (b) (0.01)	70.1	24.7	5.2	---	---	---	72	4.7
11	0.1	t-BHC (b) (0.1)	e	none	100	---	---	---	---	---	2	---
				ISL (b)	---	21.0	24.0	---	---	---	---	1.1
12	0.1	t-BHC (b) (0.1)	40-74	ISL (b)	---	48.0	41.5	4.8	5.7	---	---	1.1
13	0.1	t-BHC (b) (0.01)	78-88	BP (b) (0.01)	---	47.5	41.5	4.6	6.4	---	---	1.1
14	0.05	t-BHC (b) (0.01) (c)	45-66	ISL (b)	95.1	2.8	2.2	---	---	---	---	1.3
15	0.1	t-BHC (b) (0.08) (f)	56	ISL (b)	85.6	7.3	5.8	1.3	---	---	---	1.5

(a) See Reference 18. (b) ISL, 275 Watt Incandescent Sunlamp; BP, benzoyl peroxide, NCS, N-chlorosuccinimide. (c) In 10 ml. carbon tetrachloride. (d) In 50 ml. benzene at reflux. (e) In 60 ml. carbon tetrachloride at reflux. (f) In 20 ml. carbon tetrachloride.

TABLE II
Factors Affecting the Relative Reactivity of the Methyl Groups of 3,5-DMO

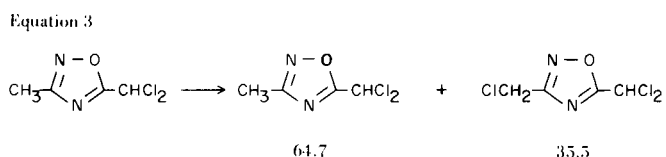
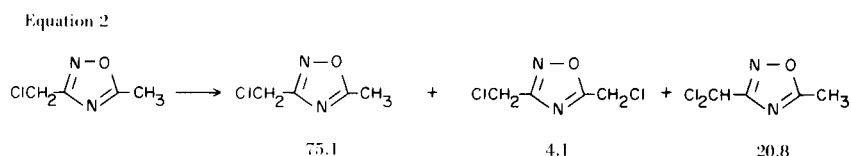
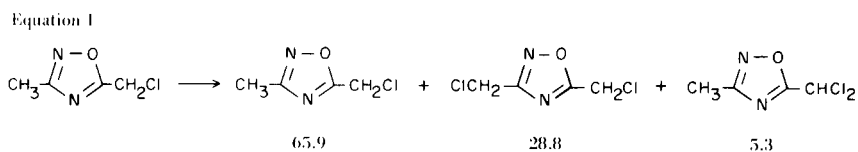
Run Number	3,5-DMO moles	CCl ₄ , ml.	Temp., °C.	Cl ₂ , Moles per Addition	Percent HCl (b) Accounted for	Additive (moles)	3,5-DMO	GLC Reaction Mixture (a), Area %	A ₃ /A ₅ (c)	Initiator
							3-ClCH ₂	5-ClCH ₂	Other	
1	0.1	25	12 ± 1	(1) 0.017 (2) 0.017 (3) 0.017	89		4	0.2	20.0	light
2	0.2	50	56 ± 1	0.042	90		12.9	2.9	4.5 (d)	light
3	0.1	50	73 ± 1	(1) 0.017 (2) 0.017	91		9.0	2.1	4.3	light
4	0.2	50	56 ± 1	0.042	34	Na ₂ CO ₃ (0.1)	10.8	2.9	4.2 (d)	light
5	0.2	50	56 ± 1	0.04		CF ₃ COOH (0.2)	11.8	2.1	5.6	light
				0.04			21.8	3.8	5.8	
				0.04			31.7	6.5		
				0.04			35.6	7.6		
				0.04			41.3	7.4		
				0.04			40.5	5.3		
6	0.1	none	56 ± 1	0.02						none (dark)
7	0.1	none	76 ± 1	0.02						none (dark)

(a) Each value the average of three determinations. (b) The sum of the acid collected in the off-gas wash plus the titrable acidity in the crude reaction mixture. (c) See Reference 18. (d) A% of 3-ClCH₂ adjusted to account for the 3-Cl₂CH present. This adjustment is used only where a trace (≤ 1 A%) of 3-Cl₂CH is observed. (e) Only in the off-gas wash.

TABLE III

Run Number	Solvent	% 3,5-DMO Converted (100-A%)	Effect of Solvent on the Chlorination of 3,5-DMO			Na ₂ CO ₃	Comments
			Time, Minutes to % Conversion	Area % 3-ClCH ₂ (A ₃)	Area % 5-ClCH ₂ (A ₅)		
1	None	4.8	205	2.7	0.8	No	1.3 A% 3-Cl ₂ CH-5-CH ₃
2	None	7.3	360	5.1	1.7	Yes	0.5 A% 3-Cl ₂ -CH-5-CH ₃
3	CCl ₄	9.3	40	8.0	1.3	No	
4	CCl ₄	15.1	40	12.4	2.7	Yes	
5	Benzene	8.4	40	6.9	1.3	No	
6	Benzene	8.9	40	7.2	1.6	Yes	
7	CS ₂	9.8	180	8.0	1.8	No	
8	CS ₂	14.9	60	12.0	2.9	Yes	

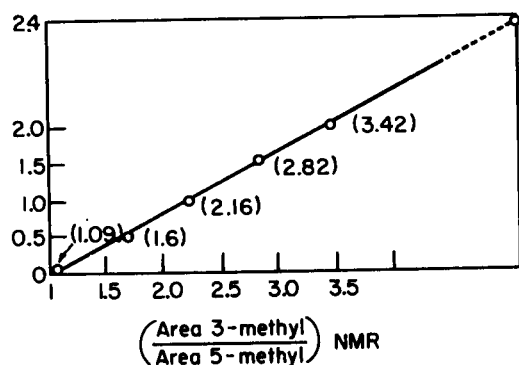
(a) See Reference 18.



The relatively greater reactivity of the 3-methyl group toward radical chlorination and the probable ionic nature of the thermal chlorination is further illustrated by the results of the photoinitiated chlorination of 3-methyl-5-chloromethyl-1,2,4-oxadiazole (Equation 1), 3-chloromethyl-5-methyl-1,2,4-oxadiazole (Equation 2), and 3-methyl-5-methyl-1,2,4-oxadiazole (Equation 3) at 40° in carbon tetrachloride. The number under each product is the area percent, approximately the mole-percent, of that material in the reaction mixture. Under these conditions neither the 5-chloromethyl nor the 5-dichloromethyl derivatives were further chlorinated at the 5-methyl group. The substituent in the 3-position is clearly more reactive.

FIGURE 1

THE DEUTERIATION OF 3,5-DMO



The effects of other chlorine sources are shown in Table I. Sulfuryl chloride behaves similarly to chlorine as does *N*-chlorosuccinimide (14). A significantly different reactivity ratio was observed in chlorinations with *t*-butyl hypochlorite when compared to that obtained with chlorine, NCS, or sulfuryl chloride. In both peroxide and light initiated reactions the reactivity ratio approximates 1.1 although in all cases the efficiency was low (15). The different reactivity ratio for *t*-BHC compared to the other chlorine sources probably lies in the chain carrier, which is in the case of *t*-BHC the *t*-butyloxy radical, while in the other cases it is the chlorine radical. Neither perchloromethanesulfonyl chloride (16) nor carbon tetrachloride (17) were effective in the chlorination of 3,5-DMO.

In limited conversion experiments (Table II) the relative reactivities of the 3- and 5-methyl groups under radical conditions were determined more precisely. It was found that the ratio of the reactivities of these groups (expressed as A_3/A_5 (18)) is temperature dependent, decreasing as temperature increases. The observation that a solid separated when either chlorine or hydrogen chloride was introduced into a carbon tetrachloride solution of 3,5-DMO at a low temperature (10-15°) led to the suspicion that the formation of a complex or a salt such as II might have an effect on the relative reactivities of the 3- and 5-methyl substituents. The addition of sodium carbonate as an acid acceptor appeared to decrease

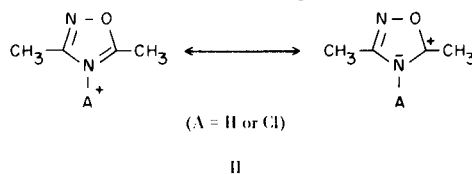


FIGURE 2

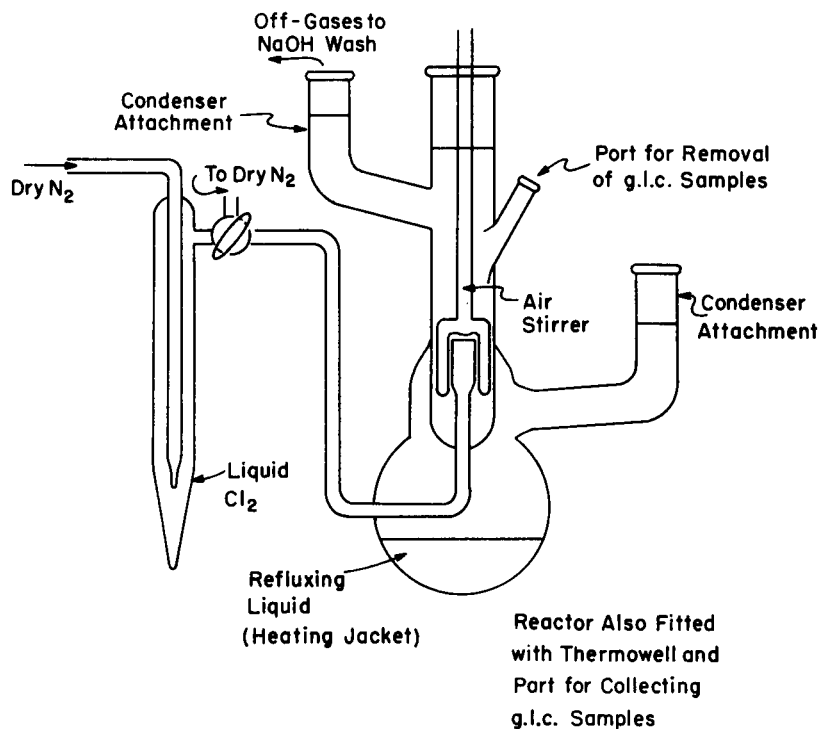
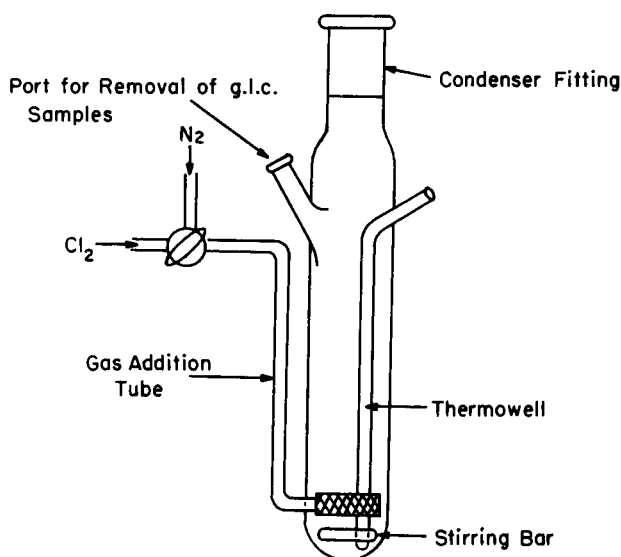


FIGURE 3



the 3-/5- reactivity ratio slightly (Tables II and III) while the addition of trifluoroacetic acid enhanced the ratio (Table II). Although the reactivity ratio differences in these cases are small, the fact that they occur regularly lends to their credibility. It was further noted that the ratio is decreased slightly with temperature increase. The importance of II (due to thermal instability) would also decrease with increasing temperature. These results are consistent with the conclusion that the role played by II in determining relative reactivities is minor.

A study of solvent effects on the relative reactivities of the 3- and 5-methyl groups (Table III) is consistent with the thought that the relative reactivity of the methyl groups in 3,5-DMO is a function of electron availability and not of the resonance stabilization of intermediates (2, 19-21).

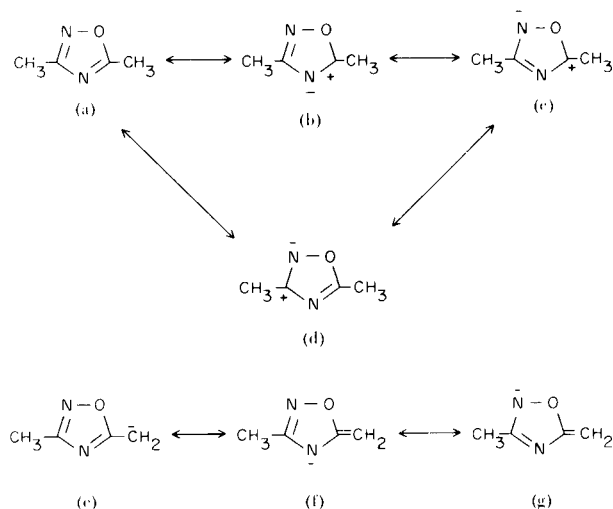
An independent demonstration that the electron availability differs at the two methyl groups of 3,5-DMO was found in nmr (ground state) and deuterium exchange studies. In carbon tetrachloride solution using tetramethyl silane as an internal standard the 3-methyl peak was found at 2.3 ppm, the 5-methyl peak at 2.53 ppm thus indicating that the 5-methyl is more deshielded

than the 3-methyl. This difference was substantiated in deuterium exchange studies where the 5-methyl was found to exchange much more rapidly than the 3-methyl in deuterium oxide solution in the presence of a trace of sodium hydroxide. In 25 hours the 5-methyl peak was no longer detectable by nmr while the 3-methyl was virtually unchanged (see Figure 1). Mass spectrographic analysis of the exchanged 3,5-DMO indicated the presence of mainly di- and tri- and no tetra-deuterated material (Table IV) at the point where a 5-methyl peak was no longer noted in nmr. The 3H/5H ratio (by mass spectra) at this point was 300/44.5 or 6.7; about 15 percent of the 5-methyl hydrogen remained. Deuterium exchange under slightly acid or neutral conditions had not proceeded to a measurable extent after 28 hours.

TABLE IV
Mass Spectrographic Analysis of
Deuterated 3,5-DMO After 28 Hours

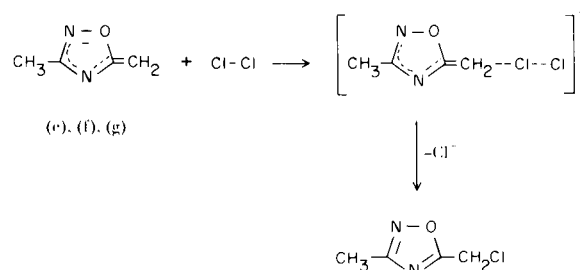
Deuteration	Mole Percent
0	0.8
1	5.3
2	31.5
3	62.3

This apparent difference in electron density and acidity between the methyl groups of 3,5-DMO is consistent with the following resonance structures. Loss of a proton from (a), (b), or (c) will result in (e), (f), and (g). Such structures are not possible when a proton is lost from (d).



It is reasonable to postulate the attack of an electrophilic chlorine molecule on (e), (f), (g) to produce the 5-chloromethyl product. Clearly, a similar mechanism could be

postulated for the further formation of the 5-di- and -tri-chloromethyl derivatives. It is probable that the effect of added sodium carbonate on A_3/A_5 (Tables II and III) is, in fact, an enhancement of the rate of ionic halogenation process.



Conclusions.

(1) In the photoinitiated (radical) chlorination of 3,5-DMO at temperatures up to 75° the 3-methyl group has been found to be 4 to 5 times more reactive than the 5-methyl group. Under these conditions both cyclohexane and toluene are chlorinated much more rapidly than is 3,5-DMO.

(2) This difference in activity has been shown to be a function of relative electron availability at the two positions.

(3) In thermally initiated reactions (about 100°) in the dark chlorination takes place at the 5-methyl group. This is most probably an ionic process. A mechanism has been postulated for this ionic reaction.

Preparation of Materials.

The chemicals used in this study are summarized in Table V. General information pertaining to the syntheses and chemical properties of 1,2,4-oxadiazole may be found in the excellent review of Eloy (22).

EXPERIMENTAL

Competition Studies Between 3,5-Dimethyl-1,2,4-Oxadiazole (3,5-DMO) and Toluene or Cyclohexane.

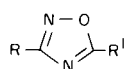
A mixture of 0.025 mole of 3,5-DMO and 0.025 mole of toluene in 20 ml. of carbon tetrachloride in a reactor shown in Figure 3 (about 30 to 40 ml. capacity) was purged with nitrogen for 15 minutes at 40 ± 2°, so maintained by a 275 W incandescent sunlamp placed an appropriate distance from the reactor, and then treated with chlorine at a flow rate (12) equal to 0.8 g./hour. After 4 hours a glc scan gave the following results (in area percent): 3,5-DMO, 42; monochlorinated 3,5-DMO, 4.6; benzylchloride, 31.5; benzal chloride, 21.9; benzotrichloride, trace. A study of a mixture consisting of 0.5 ± 0.05 g. of 3,5-DMO, 3-chloromethyl-5-methyl-1,2,4-oxadiazole, benzylchloride and benzal chloride in four volumes of carbon tetrachloride indicated that the major components of the product mixture gave about the same molar response in glc. The study with cyclohexane involved 0.025 mole of 3,5-DMO and 0.0125 mole cyclohexane under the same

conditions as above except that the reaction was conducted for only 150 minutes. A glc scan gave the following results (in area percent): 3,5-DMO, 80.5; monochlorinated 3,5-DMO, 4.6; chlorocyclohexane, 3.9; and two small peaks which were assigned to be di and/or poly-chlorocyclohexane.

Gross Effect of Light and Temperature on the Chlorination of 3,5-DMO (Table I).

The reactions involving chloring in Table I performed in a reactor similar to that shown in Figure 2, but the chlorine was passed directly from the tank through a sulfuric acid bath into the reactor at a rate held at 6 ml./minute (sapphire ball rotometer).

TABLE V
Various Substituted 3,5-Dimethyl-1,2,4-Oxadiazoles
Used in This Study



Number	R	R ¹	Reference
I	CH ₃	CH ₃	a
II	ClCH ₂	CH ₃	c
III	CH ₃	CH ₂ Cl	b
IV	Cl ₂ CH	CH ₃	c
V	ClCH ₂	CH ₂ Cl	c
VI	CH ₃	CHCl ₂	b
VII	Cl ₃ C	CH ₃	c
VIII	Cl ₂ CH	CH ₂ Cl	c
IX	ClCH ₂	CHCl ₂	b
X	CH ₃	CCl ₃	b
XI	Cl ₃ C	CH ₂ Cl	c
XII	Cl ₂ CH	CHCl ₂	c
XIII	ClCH ₂	CCl ₃	b
XIV	Cl ₃ C	CHCl ₂	c
XV	Cl ₂ CH	CCl ₃	c
XVI	Cl ₃ C	CCl ₃	c

(a) Reference 23. (b) Reference 24. (c) A sample was supplied by R. Lenaers, Union Carbide European Research Associates, Brussels, Belgium.

The conditions are shown in Table I. The reaction mixtures were purged with nitrogen for 15 minutes prior to chlorination.

The reaction temperatures were maintained by refluxing the following materials in the heating jacket: 46-48°, carbon disulfide; 74°, carbon tetrachloride; 106°, toluene.

The low temperature reactions were carried out in a reactor similar to Figure 2 immersed in a cooling bath.

The analytical data were obtained by glc of the reaction mixture at the time indicated.

Effects of Various Factors on the Relative Reactivities of the 3- and 5-Methyl Groups (Table II).

The reactions were carried out in the reactor shown in Figure 2 using the conditions described in Table II. For the 56° reaction

temperature refluxing acetone was employed, carbon tetrachloride for the 76° reaction temperature, and a temperature of 12° was obtained by circulating tap water through the external jacket. The light source was a 275 W incandescent sunlamp in a constant position 6 inches from the reactor.

The dry chlorine (sulfuric acid bath) was collected in the indicated tube, the reaction mixture was heated to temperature, purged for 15 minutes with dry (sulfuric acid bath) nitrogen with stirring and then the chlorine was swept in over about one hour with dry nitrogen. Nitrogen purging was continued 30 minutes after chlorine addition was complete.

The off-gas from the reaction was passed through standard sodium hydroxide and, at the end of the addition period, this solution was back-titrated in order to determine the total acidity in the off-gas. An aliquot of the reaction mixture in methanol was also titrated rapidly in the cold to determine total acidity.

In the experiments where additives were used the material was placed in the reaction mixture prior to purging.

Analyses of the final reaction mixture were carried out by glc.

Solvent Effects on the Relative Reactivities of the 3- and 5-Methyl Groups (Table III).

A solution of 0.05 mole of 3,5-DMO in 20 ml. of solvent in the reactor (30-40 ml. capacity) shown in Figure 3 was irradiated with a 275 W incandescent sunlamp set at such a distance that the temperature for the reactor was maintained at 40 ± 2°. The reaction mixture was then purged with nitrogen for 15 minutes and then chlorine (dried through sulfuric acid) was passed in for the time indicated. When addition was complete the mixture was analyzed by glc.

In experiments where sodium carbonate was employed, 0.01 mole of this material was added prior to the initial nitrogen purge.

The Chlorination of 3,5-DMO with Sulfuryl Chloride (Table I).

Mixtures of 3,5-DMO and sulfuryl chloride in the proportions indicated in Table I, with or without solvent, were placed in a 100 ml. flask fitted with a reflux condenser, thermometer, and a stirring bar. The conditions for each run are described in the table.

In the first light-catalyzed experiment a 275 W incandescent sunlamp was placed at such a distance from the reactor as to hold the temperature at 40 ± 2°.

In the second light-catalyzed experiment the temperature was increased slowly by heating with heating mantle while the light was kept a constant distance from the flask. The flask was heated at 100° until sulfur dioxide and hydrogen chloride evolution ceased.

In the last two experiments a reactor similar to that in Figure 2 but with no addition tube was employed. The reaction mixture was changed, the reactor wrapped with aluminum foil to exclude light, and the mixture was heated with toluene refluxing in the heating jacket. Due to sulfur dioxide and hydrogen chloride evolution and sulfuryl chloride reflux the reaction temperature remained at about 72° until the reaction was nearly complete when it rose rather rapidly to 106°. In the benzoyl peroxide initiated experiment, 0.01 mole of initiator was added to the original charge.

The analyses of the final reaction mixtures were carried out by glc.

Chlorination of 3,5-DMO with Agents Other Than Chlorine (Table I).

The reactants in the designated amounts with or without solvents were mixed in a 100 ml. flask fitted with a condenser, a thermometer, and a stirring bar. The reactions were carried out

TABLE VI
 GLC Analyses of Chlorination of 3,5-DMO

Compound	A%	A% ox/A% CCl ₄	Moles, x 10 ³	M ox/M CCl ₄	Total Moles Contained	Weight, g.	Cl Equivalent, g.
Known Mixture:							
CCl ₄	9.8	1	1.62	1			
3,5-DMO	29.6	3.02	5.1	3.15			
5-ClCH ₂	24.8	2.53	3.8	2.35			
5-Cl ₂ CH	21.6	2.20	3.0	1.85			
5-Cl ₃ C	14.4	1.44	2.5	1.54			
Reaction Mixture:							
CCl ₄	31.70	1	1.62 (a)	1	0.31 (c)	30.4 (d)	0 (e)
3,5-DMO	50.49	1.59	2.7	1.66 (b)	0.014	1.9	0.44
5-ClCH ₂	2.64	0.08	0.12	0.074	0.007	0.95	0.22
3-ClCH ₂	1.37	0.04	0.06	0.037	0.057	0.95	0.43
5-Cl ₂ CH	1.17	0.037	0.05	0.031	0.081	16.3	8.5
5-Cl ₃ C	12.62	0.4	0.7	0.43		50.50	9.6

(a) $1.62 \times (M \text{ ox}/M \text{ CCl}_4) \text{ reaction} = M \times 10^3$ in 0.5 g. reaction mixture. (b) Based on relationship $(A\% \text{ ox}/A\% \text{ CCl}_4) \text{ known} = \frac{(A\% \text{ ox}/A\% \text{ CCl}_4) \text{ reaction}}{(M \text{ ox}/M \text{ CCl}_4) \text{ reaction}}$

115 x (M x 10³). (d) Total moles contained x MW. (e) Total weight x % Cl in molecule.

under the conditions described in Table I. The results of the various runs are described in Table I. The analyses were carried out using glc.

The Thermal Chlorination of 3,5-DMO.

The reaction was carried out in the reactor shown in Figure 2.

A charge of 50 g. (0.5 mole) of 3,5-DMO was placed in the reactor and the toluene in the heating jacket was heated at reflux so that the reactor maintained an internal temperature of 104°. The hot reaction mixture was purged with dry nitrogen for 20-30 minutes with gentle stirring, the reactor was then wrapped with aluminum foil to protect it from light, and chlorine addition was initiated by passing a gentle stream of dry nitrogen through 30.2 g. (0.42 mole) chlorine in the chlorine trap. Approximately 3 hours were required for this addition. Throughout the reaction the off-gases were passed through standard sodium hydroxide solution. When addition was complete nitrogen purge was continued for 20 minutes. During the reaction a small amount of solid collected in the lower portion of the condenser. The analyses are discussed below.

An analysis of the off-gas revealed that 532 meq of acid was collected; theory 425 mgq. Thus, 76 percent (0.32 mole) of the available chlorine was involved in the reaction.

Reaction Mixture Analysis.

The total product in the kettle weighed 58 g. Rapid titration with standard sodium hydroxide solution indicated that this product contained no more than 0.5 g. hydrogen chloride. Assuming the absorption of 0.32 A of chlorine the theoretical weight for the reaction mixture was 61.05 g.; $58/61.05 \times 100 = 95$ percent recovery.

The reaction mixture was analyzed for total chlorine: *Anal.* Calcd.: 19.6. Found: 22.55.

The reaction mixture was submitted to detailed glc analysis (Table VI). A solution of 0.5 g. of the reaction mixture in 0.25 g. of carbon tetrachloride was analyzed by glc. A solution of 0.5 g. each of 3,5-DMO and the three 5-chloroderivatives of 3,5-DMO in 0.25 g. carbon tetrachloride was also analyzed by glc. The mathematical analyses of those mixtures is presented in Table VI. By this method 50.5 g. (88%) of the total product weight and 9.6 g. (83%) of the total chlorine is accounted for.

Analyses of Solid in the Condenser.

This amounted in weight to 4 g. It was suspended in methylene chloride and allowed to dissolve during which process a mixture of hydrogen chloride and chlorine was evolved. The methylene chloride solution was analyzed by glc and was found to contain only 3,5-DMO. Since the stoichiometry of this material is not known this 4 g. was not included in the calculations of efficiency.

Photoinitiated Chlorination of Chloro Derivatives of 3,5-DMO, Equations (1), (2), and (3).

A solution of 0.05 mole of the appropriate oxadiazole in 20 ml. carbon tetrachloride was placed in a reactor similar to that shown in Figure 3. The chlorine came directly from the tank and was dried through concentrated sulfuric acid.

The mixture was heated to reflux with a 275 W incandescent sunlamp and purged with nitrogen for 15 minutes and then the temperature was adjusted to $40 \pm 2^\circ$ by proper placement of the sunlamp and chlorine was passed into the reaction at a relative flow rate of 108 mm (U-tube flow meter) for 1.5 hours in the cases of the monochloro compounds and for 3 hours in the case of the dichloro compound. Analyses of the reaction mixtures were

accomplished by glc. The results are shown in the text (Equations 1, 2, and 3).

REFERENCES

- (1) C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, **82**, 6113, 6108 (1960).
- (2) C. Walling and B. Miller, *ibid.*, **79**, 4181 (1957).
- (3) G. A. Russel and R. C. Williamson, Jr., *ibid.*, **86**, 2357 (1964).
- (4) R. D. Gilliom and B. F. Ward, Jr., *ibid.*, **87**, 3944 (1965).
- (5) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, 1957, pp. 361 ff.
- (6) F. R. Mayo and C. Walling, *Chem. Rev.*, **46**, 1919 (1950).
- (7) G. A. Russel, *J. Am. Chem. Soc.*, **89**, 4997 (1958).
- (8) S. D. Sokolov and N. K. Kochetkov, *J. Gen. Chem. USSR (Eng. Trans.)*, **33**, 1170 (1962).
- (9) B. M. Mikhailov and V. P. Bronovitskoya, *ibid.*, **27**, 799 (1957).
- (10) R. Gompper and H. Ruhle, *Ann. Chem.*, **626**, 83, 92 (1960).
- (11) P. Beltrame and S. Carra, *Tetrahedron Letters*, **44**, 3909 (1965).
- (12) G. Benoy and J. C. Jungers, *Bull. Soc. Chim. Belg.*, **65**, 769 (1956); *Chem. Abstr.*, **51**, 9330 (1957).
- (13) G. A. Russell and H. C. Brown, *J. Am. Chem. Soc.*, **77**, 4578 (1955); H. C. Brown and G. A. Russell, *ibid.*, **74**, 3995 (1952).
- (14) C. Walling and A. L. Rieger, *ibid.*, **85**, 3134 (1963).
- (15) Because of the low reactivity of 3,5-DMO toward *t*-BHC the usual competing reaction in *t*-BHC chlorinations (breakdown to acetone and methyl chloride, followed by formation of chloroacetone) was observed to compete quite successfully with the desired reaction. M. Anbar and D. Ginsburg, *Chem. Rev.*, **54**, 925 (1954).
- (16) E. S. Huyser and B. Giddings, *J. Org. Chem.*, **27**, 3391 (1962).
- (17) S. Winstein and F. H. Seabold, Jr., *J. Am. Chem. Soc.*, **69**, 2961 (1947).
- (18) A₃ is the area percent of 3-chloromethyl-5-methyl-1,2,4-oxadiazole and A₅ the area percent of 5-chloromethyl-3-methyl-1,2,4-oxadiazole observed on a glc scan. Since it has been determined that these materials give essentially identical molar responses on glc, A₃/A₅ may be taken as a measure of the relative reactivities of the 3,5-DMO methyl groups in the present reaction.
- (19) R. Van Helden and E. C. Kooyman, *Rec. Trav. Chim.*, **73**, 269 (1954).
- (20) H. Magritte and A. Bruylants, *Bull. Soc. Chim. Belges*, **66**, 367 (1957).
- (21) A. Bruylants *et al.*, *Ind. Chem. Belges*, **20**, Spec. No. 2 588 (1955) *Chem. Abstr.*, **50**, 7718 (1956).
- (22) F. Eloy, *Fortschr. Chem. Forsch.*, **4**, 812 (1965).
- (23) J. A. Durden, Jr. and D. L. Heywood, *J. Org. Chem.*, **30**, 4359 (1965).
- (24) A. A. Sousa, H. C. Chitwood, and J. A. Durden, Jr., U.S. Patent 3,192,103 (to Union Carbide Corporation), June 29, 1965.
- (25) The vpc analyses were carried out on an Aerograph A-90 chromatograph using a 10-foot 10 percent Dow 710 silicone on chromosorb W column at 18 psig helium flow and 150°, the nmr analyses were obtained with a Varian A-60 instrument.