Relative Rates of Addition of Iodine Isocyanate to Unsaturated Compounds[1]

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The relative rates of addition of iodine isocyanate (generated *in situ* from iodine and silver cyanate) to unsaturated compounds was studied with 18 unsaturated compounds at a temperature range from −80 to 3°, over a range of concentrations, and at various ratios of reactants. Rates of reaction decrease with decreasing temperature and concentration of unsaturated compound and also when excess olefin is used. Vinyl and isopropenyl acetates react very rapidly whereas alkynes react slowly. When an electron-withdrawing carbonyl group or chlorine atom is attached to the double bond, essentially no reaction occurs. The relative rates of addition of *in situ* generated iodine isocyanate to unsaturated compounds follows a series typical of an electrophilic reaction.

The pioneering work of Birckenbach and Linhard[3] showed that iodine isocyanate adds to olefinic double bonds in a manner typical of pseudo-halogens. Recently Drefahl and Ponsold[4] showed that the isocyanate group becomes attached to the more alkyl- (or aryl-) substituted olefinic carbon in substituted cyclohexenes, and Hassner and Heathcock[5] obtained a similar result in acyclic systems. Both groups demonstrated that the reaction occurs in a stereospecific *trans* manner, and suggested that an iodonium ion is involved as an intermediate.[4,5] The addition products are vicinal iodoisocyanates.

While iodine isocyanate appears to behave as an electrophilic agent, there is little information available concerning its relative reactivity with olefins of varying nucleophilic character. Birckenbach and Linhard[3] had qualitatively noted that the addition of iodine isocyanate to ethylene was much slower than to either cyclohexene or 2-methyl-2-butene. Experimentally, this problem can be studied with solutions of preformed iodine isocyanate or by generating this reagent *in situ* from silver cyanate and iodine in the presence of the olefin. The use of preformed iodine isocyanate solutions offers certain obvious advantages over the heterogeneous *in situ* method and some preliminary studies have been reported.[6] Nonetheless, the *in situ* method is more commonly used in synthetic procedures and a detailed knowledge of the relative reactivities under these experimental conditions is highly desirable.

In a preliminary communication[1b] we reported that there is a strong similarity among the relative electrophilicities of iodine isocyanate (generated *in situ*), dibromocarbene, and bromine. We now wish to report the relative rates of the addition of iodine isocyanate, generated *in situ* under heterogeneous conditions, to a wide variety of unsaturated compounds and to assess the synthetic utility of this reaction.

Experimental Section

Melting points were determined with a Thomas–Hoover apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Infracord 137 and were run as Nujol mulls. Kinetic results were monitored with an F & M scientific model 500 gas chromatograph equipped with a disk integrator using columns and conditions appropriate to the compounds studied. Microanalyses were performed by Microanalysis Laboratories, Wilmington, Del.

Unsaturated compounds and internal standards were shown to be pure by glpc analysis. The iodine was Fisher or Baker resublimed grade; silver cyanate was from Eastman Organic Chemical Co.

General Procedure.—Reactions were run in a semimicro, four-necked flask fitted with a condenser and/or drying tube, an electrically driven stirrer with a Teflon blade, a thermometer, and a rubber septum through which samples could be removed for analysis. The entire apparatus was wrapped in aluminum foil to exclude light.

The requisite amounts of anhydrous ether, iodine, olefin, and an internal standard were placed in the flask which was then sealed and immersed in a dewar flask containing a freezing methanol–water solution. About four–eight replicate samples (~ 3 μl) of this solution were removed through the rubber septum *via* a hypodermic syringe and the glpc areas of the unsaturated compound and internal standard were computed. The use of the internal standard (generally this was approximately 40% by weight, based on unsaturated compound, of benzene, toluene, or a suitable saturated aliphatic hydrocarbon) permitted ready determination of unreacted unsaturated compound during the course of the reaction. Column conditions and stationary phases chosen depended on the compounds studied; however, most unsaturated hydrocarbons were monitored using a 20-ft column with 15% Apiezon L on Anakrom ABS 70/80 mesh. The more polar unsaturated compounds were monitored with silicone SE 30 or Carbowax 20M-terephthalate columns. Ordinarily, good agreement was found between the initial ratio of internal standard and that computed from glpc curves.

After the iodine–unsaturate–ether solution had attained thermal equilibrium, dry silver cyanate was added in one portion with stirring. Samples for glpc analysis were removed periodically through the rubber septum. (During sampling, stirring was discontinued for approximately 30 sec to permit the insoluble silver salts to settle.) Whenever possible, reactions were followed until over 90% of the unsaturated compound had disappeared. Nonreactive compounds were run for at least 24 hr.

The reaction conditions for the kinetic runs are summarized in Table I. Figures 1–5 show plots of the extent of reaction (measured by disappearance of unsaturated compound) against time in minutes. The rate data are reproducible and have been repeated many times.

General Isolation Procedure.—In most cases, after completion of the kinetic runs the solutions were filtered and the bulk of the ether was removed by evaporation. At this point, infrared spectra showed a strong band at 2250 cm^{-1} due to the presence of an organic isocyanate. In some cases, the vicinal iodoisocyanates were converted into methyl iodocarbamates by refluxing in methanol (30–45 min for secondary isocyanates and 5–6 hr for tertiary isocyanates) until that infrared band had disappeared. The bulk of the methanol was then evaporated and the residual sample was treated with a large quantity of dilute aqueous sodium sulfite to remove traces of iodine and to precipitate the iodocarbamate which was then filtered off, if solid, or extracted with ether. These compounds could usually be further purified by recrystallization from methanol or acetone. Infrared spectra of vicinal methyl iodocarbamates showed N—H bands at about 3200 and 1500 cm^{-1} and a C═O band at about 1650 cm^{-1}.

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(1) (a) Pseudo-Halogens. II. (b) For part I, see C. G. Gebelein and D Swern, *Chem. Ind.* (London), 1462 (1965). (c) Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965. (d) This work was partially supported by Public Health Service Research Grants No. CA-07803 and CA-07174.

(2) Work submitted in partial fulfillment of the requirements for the Ph.D. degree, Temple University, Feb 1967.

(3) L. Birckenbach and M. Linhard, *Ber.*, **63**, 2544 (1930); **64**, 961, 1076 (1931).

(4) G. Drefahl and K. Ponsold, *Chem. Ber.*, **93**, 519 (1960); G. Drefahl, K. Ponsold, and G. Köllner, *J. Prakt. Chem.*, **23**, 136 (1964).

(5) A. Hassner and C. C. Heathcock, *Tetrahedron Lett.*, 1125 (1964).

(6) S. Rosen and D. Swern, *Anal. Chem.*, **38**, 1392 (1966).

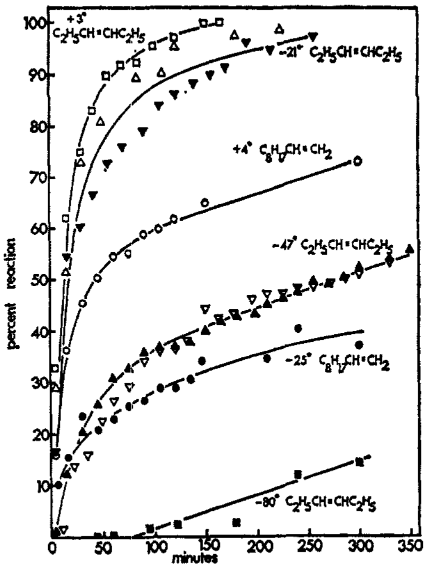

Figure 1.—Effect of temperature on the reaction rate of 0.25 M 1-decene and 0.15 M *trans*-3-hexene with iodine isocyanate: 1-decene at 4°, ○; 1-decene at −25°, ●; *trans*-3-hexene at 3°, □; *trans*-3-hexene at −21°, △▼; *trans*-3-hexene at −47°, ▲▽; *trans*-3-hexene at −80°, ■.

TABLE I

ADDITION OF IODINE ISOCYANATE, GENERATED *in situ*, TO UNSATURATED COMPOUNDS

Unsaturated compound	Molarity	Molar ratio, AgOCN/I_2/ unsaturate	Reacn temp, ±1°C	Figure
1-Hexene	0.500	1.33/1.00/1.00	4[a]	2
1-Decene	0.262	1.31/1.00/1.03	−25	1
1-Decene	0.246	1.30/1.00/0.96	4	1
Vinyl acetate	0.137	1.30/1.00/1.67	−47	4
Vinyl acetate	0.135	1.29/1.00/0.65	−48	4
Vinyl acetate	0.500	1.33/1.00/1.00	−20[b]	
Isopropenyl acetate	0.145	1.28/1.00/0.70	−47	4
Isobutyl vinyl ether	0.139	1.28/1.00/0.67	−48	
Methyl vinyl ketone	0.500	1.33/1.00/1.00	1[c]	
Methyl methacrylate	0.500	1.33/1.00/0.50	−25[c]	
2-Methyl-1-pentene	0.137	1.29/1.00/0.66	−47	3
2-Methyl-1-pentene	0.500	1.33/1.00/1.00	3[a]	2
trans-3-Hexene	0.146	1.28/1.00/0.70	−80	1
trans-3-Hexene	0.137	1.29/1.00/0.66	−48	1, 3, 4
trans-3-Hexene	0.145	1.28/1.00/0.70	−22	1, 3
trans-3-Hexene	0.150	1.32/1.00/0.73	3	1
trans-3-Hexene	0.500	1.33/1.00/1.00	1[a]	2
Ethyl crotonate	0.500	1.33/1.00/1.00	4[c]	
2,3-Dimethyl-2-butene	0.137	1.29/1.00/0.66	−47	3
2,3-Dimethyl-2-butene	0.142	1.29/1.00/0.68	−47	3
3-Hexyne	0.500	1.33/1.00/1.00	4	2
Cyclopentene	0.141	1.28/1.00/0.67	−22	5
Cyclohexene	0.135	1.33/1.00/0.67	−22	3, 5
Cyclohexene	0.500	1.33/1.00/1.00	1[a]	2
Cycloheptene	0.136	1.29/1.00/0.66	−23	5
Cycloheptene	0.500	1.33/1.00/1.00	−19[a]	
Cycloheptene	0.500	1.33/1.00/1.00	2[a]	2
Cycloctene	0.134	1.28/1.00/0.64	−23	5
Norbornene	0.141	1.28/1.00/0.67	−21	5

[a] In these more concentrated solutions, an exotherm of 4–6° was noted. [b] An exotherm of 22° occurred in this run. The solvent was tetrahydrofuran. [c] When no reaction was observed after 5 hr, the reaction system was allowed to warm to room temperature and was monitored for at least 24 hr.

In certain cases, the vicinal iodoisocyanates were converted into the corresponding iodoamine hydrochlorides by adding concentrated aqueous hydrochloric acid to the ethereal solution and stirring sevaral hours. After evaporation to dryness, the iodoamine hydrochloride was recrystallized from ethanol. The ir spectra showed the typical NH_3^+ bands at 2400–2600 cm^{-1}.

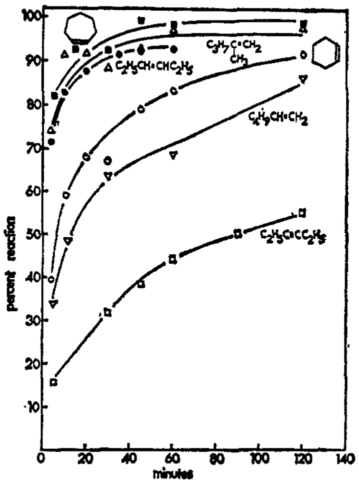

Figure 2.—Rate of addition of iodine isocyanate to various unsaturated compounds at 1–4°, 0.50 M unsaturate, and a molar ratio of AgOCN/I_2/unsaturate of 1.33/1.00/1.00: ■, cycloheptene; △, 2-methyl-1-pentene; ●, *trans*-3-hexene; ○, cyclohexene; ▽, 1-hexene; □, 3-hexyne.

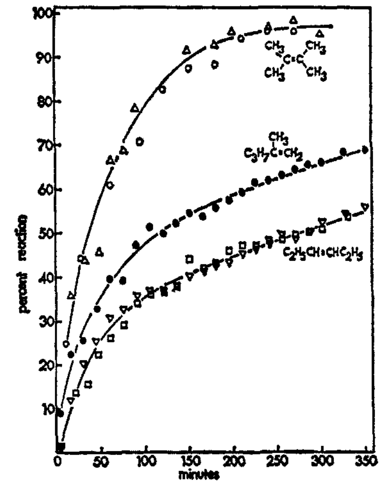

Figure 3.—Rate of addition of iodine isocyanate to *trans*-3-hexene, 2-methyl-1-pentene, and 2,3-dimethyl-2-butene at −47°, 0.14 M olefin, and an average AgOCN/I_2/olefin ratio of 1.29/1.00/0.67.

Preparative Runs.—Preparative runs were made in several cases using the general procedure described by Hassner and Heathcock.[7,8] Iodoisocyanates were converted into the corresponding carbamates or amine hydrochlorides in the usual fashion.

Methyl (*trans*-2-iodocyclohexyl)carbamate was prepared from cyclohexene, mp 133.0–133.7° from acetone (lit.[3] mp 135°).

Methyl (*trans*-2-iodocyclopentyl)carbamate was prepared from cyclopentene, mp 81–83° from methanol (lit.[7,8] mp 85–87°).

Anal. Calcd for $C_7H_{12}NO_2I$: C, 31.25; H, 4.50; N, 5.21; I, 47.16. Found: C, 31.39; H, 4.64; N, 4.79; I, 46.05.

4,5-Trimethylene-2-oxazolidone was prepared from methyl (*trans*-2-iodocyclopentyl)carbamate by mild heating in a manner similar to that described by Heathcock and Hassner,[9] mp 87–88° from acetone.

Anal. Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.75; H, 6.90; N, 10.98.

Methyl (*trans*-2-iodocycloheptyl)carbamate was prepared from cycloheptene, mp 103.5–104.5° from methanol (lit.[7,8] mp 103–104°).

Anal. Calcd for $C_9H_{16}NO_2I$: C, 36.38; H, 5.43; N, 4.71; I, 42.71. Found: C, 36.36; H, 5.28; N, 4.61; I, 42.55.

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(7) A. Hassner and C. Heathcock, *Tetrahedron*, 1037 (1964).

(8) A. Hassner, M. E. Lorber, and C. Heathcock, *J. Org. Chem.*, **32**, 540 (1967).

(9) C. Heathcock and A. Hassner, *Angew. Chem. Intern. Ed. Engl.*, **2**, 213 (1963).

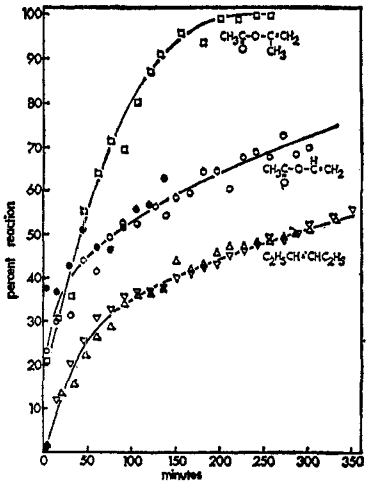

Figure 4.—Rate of addition of iodine isocyanate to *trans*-3-hexene, vinyl acetate, and isopropenyl acetate at −47°, 0.14 *M* of unsaturate, and an average AgOCN/I_2/unsaturate ratio of 1.29/1.00/0.67.

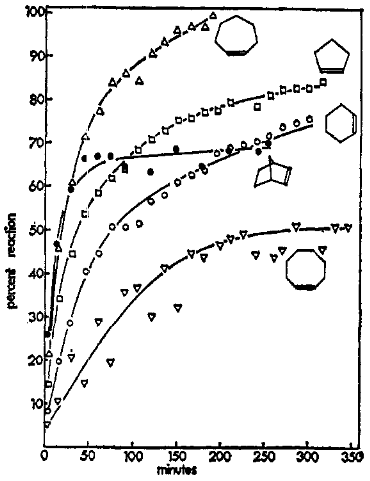

Figure 5.—Rate of addition of iodine isocyante to cyclic olefins at −22°, 0.14 *M* olefin, and an average AgOCN/I_2/olefin ratio of 1.29/1.00/0.66: □, cyclopentene; ○, cyclohexene; △, cycloheptene; ▽, cyclooctene; ●, norbornene.

Methyl (*trans*-2-iodocyclooctyl)carbamate was prepared from cyclooctene, mp 117.8–118.4° from methanol (lit.[7,8] 115–116.5°).

Anal. Calcd for $C_{10}H_{18}NO_2I$: C, 38.60; H, 5.83; N, 4.50; I, 40.78. Found: C, 38.77; H, 5.78; N, 4.48; I, 40.85.

Methyl (2-iodocyclododecyl)carbamate was prepared from cyclododecene (33% *cis*- and 67% *trans*-), mp 103.8–104.9° from methanol (lit.[7,8] mp 102–104°).

Anal. Calcd for $C_{14}H_{26}NO_2I$: C, 45.79; H, 7.14; N, 3.81; I, 34.55. Found: C, 45.95; H, 7.24; N, 3.76; I, 34.29.

Methyl [1-(iodomethyl)heptyl]carbamate was prepared from 1-octene, mp 48.0–48.9° from methanol.

Anal. Calcd for $C_{10}H_{20}NO_2I$: C, 38.35; H, 6.44; N, 4.47; I, 40.52. Found: C, 38.41; H, 6.42; N, 4.47; I, 40.69.

4-Iodo-3-aminohexane hydrochloride was prepared from *trans*-3-hexene, mp 147.5–149.0 from ethanol.

Anal. Calcd for $C_6H_{15}NICl$: C, 27.35; H, 5.74; N, 5.32. Found: C, 27.58; H, 5.66; N, 5.12.

3-Iodo-2-amino-2,3-dimethylbutane hydrochloride was prepared from 2,3-dimethyl-2-butene, mp >330° from ethanol.

Anal. Calcd for $C_6H_{15}NICl$: C, 27.35; H, 5.74; N, 5.32. Found: C, 26.93; H, 5.99; N, 5.43.

Results

Figures 1–5 summarize the results of heterogeneous kinetic studies on the addition of iodine isocyanate, generated *in situ*, to a variety of unsaturated compounds at different temperatures, concentrations, and reactant ratios. In all figures, the extent of reaction is expressed as the per cent of unsaturated compounds consumed in a given time interval.

Figure 1 shows that *in situ* generated iodine isocyanate reacts faster with *trans*-3-hexene than with 1-decene, even though the latter was employed at a higher molarity. Figure 1 also shows that the rate of reaction decreases with decreasing temperature.

The effects of structure of the unsaturated compound is seen in Figure 2 which shows the reaction of five olefins and one acetylene with iodine isocyanate at 1–4°. The disubstituted 1-olefin, 2-methyl-1-pentene, reacts faster than the internal *trans* olefin, *trans*-3-hexene, and the monosubstituted olefin, 1-hexene. Internal olefins show considerable variation in rate. The difference in reactivity of the fastest reacting olefins can not be ascertained accurately at this temperature and concentration, however. The internal acetylene, 3-hexyne, was slower than 1-hexene.

When the temperature is lowered still further to −47°, as shown in Figure 3, the difference between 2-methyl-1-pentene and *trans*-3-hexene becomes evident. Under these conditions, the very reactive 2,3-dimethyl-2-butene can be studied. This last olefin is the most reactive olefin studied.

Iodine isocyanate also adds to unsaturated compounds other than olefins and acetylenes. Vinyl and isopropenyl acetates both react rapidly. At −47° and 0.14 *M*, the rates of reaction of vinyl and isopropenyl acetates can be conveniently studied, as shown in Figure 4. Isopropenyl acetate reacts faster than vinyl acetate and about as fast as 2,3-dimethyl-2-butene. Vinyl acetate reacts slightly more slowly than 2-methyl-1-pentene, but faster than *trans*-3-hexene.

Figure 5 shows the reaction of five cyclic olefins with iodine isocyanate at −22°. The order of increasing rate of reaction is cyclooctene < cyclohexene < cyclopentene < cycloheptene = norbornene (initial rate).

Methyl oleate and methyl elaidate (*cis*- and *trans*-methyl-9-octadecenoate, respectively) both react about as rapidly as *trans*-3-hexene at 3° and 0.15 *M*.

Unsaturated compounds, such as methyl vinyl ketone, methyl methacrylate, ethyl crotonate, and vinylidene chloride do not appear to react with iodine isocyanate. Polyunsaturated compounds, such as dienes, do react with iodine isocyanate. Preliminary results indicate that dienes do not always react with 2 mol of iodine isocyanate; this is in agreement with Birckenbach's[3] observation that isoprene reacts with only 1 mol of iodine isocyanate.

Discussion

Figures 1–5 show that different unsaturated compounds display widely different reactivity with iodine isocyanate under the reaction conditions studied. While a qualitative ranking can readily be made on the basis of these data, a quantitative approach offers several advantages. These include the possibility of assessing the effect of alkyl group loading on the reactivity of the double bond, the effect of ring size in cyclic systems, and a comparison of the iodine isocyanate reactions with other electrophilic reactions.

Relative Reactivity Determinations.—The most direct method of obtaining a quantitative series is to compare the specific rate constants for the individual systems. The heterogeneous system, however, does not lend itself to a true kinetic study. The results obtained do not follow first-, second-, or third-order kinetics.

The addition reaction does not depend primarily on the rate of generation of iodine isocyanate from iodine and silver cyanate. Solutions of iodine isocyanate react very rapidly with many olefins.[6] If generation of iodine isocyanate were the controlling factor, there should be less marked differences observed among the various unsaturated compounds studied; this is in contrast to the results in Figures 1–5. In addition, many olefins (for example, *trans*-3-hexene at −22°) add iodine isocyanate faster than it is generated in solutions containing no olefin.[6]

Table II summarizes the results of four different sets of reaction conditions that had been used to span the wide reactivity range of compounds studied. The agreement between the value of 570 for *trans*-3-hexene at −22° and 580 for this olefin at +1° indicates that the method used here is at least internally consistent. The most important conclusion from Table II is that the presence of an electron-withdrawing group adjacent to the double bond retards the reaction while electron-donating groups accelerate it. Thus, the electron-withdrawing carbonyl groups in methyl vinyl ketone, methyl methacrylate, and ethyl crotonate, and the chlorine atoms in vinylidene chloride effectively preclude addition of iodine isocyanate to these compounds. On the other hand, the reactivity shows a pronounced increase as the number of electron-donating alkyl groups about the double bond increases. These results are typical of an electrophilic reaction, and are consistent with the proposals of Drefahl and Ponsold[4] and of Hassner and Heathcock.[5]

TABLE II

RELATIVE REACTIVITIES OF UNSATURATED COMPOUNDS WITH IODINE ISOCYANATE (GENERATED *in Situ* UNDER HETEROGENEOUS CONDITIONS) AT VARIOUS TEMPERATURES AND CONCENTRATIONS[a,b]

	Molarity of unsaturated compd				
Compound	$0.14^{b,c}$	0.15^{d}	0.50^{e}	$0.15^{b,f}$	Average rel reactivity
2,3-Dimethyl-2-butene	3800				3800
Isopropenyl acetate	3700				3700
Vinyl acetate	1950				1950
2-Methyl-1-pentene	1250				1250
Methyl oleate				570	570
trans-3-Hexene		570	580		570
Methyl elaidate				500	500
Norbornene		440			440
Cycloheptene		430			430
Cyclopentene		220			220
Cyclohexene		100	100		100
1-Hexene			50		50
Cyclooctene		35			35
3-Hexyne			8.0		8
Methyl vinyl ketone			0		0
Vinylidene chloride			0		0
Methyl methacrylate			0		0
Ethyl crotonate			0		0

[a] Since a comparison of the relative reactivities could not be made using specific kinetic rate constants, an alternate procedure was used. We have computed the reciprocal time in minutes to achieve equivalent extents of reaction and normalized these data on a scale in which cyclohexene is assigned the arbitrary value of 100. These normalized reciprocal times were computed at intervals of 5% reaction and were averaged to yield the relative reactivity values for the unsaturated compounds studied. [b] The base point for these conditions was *trans*-3-hexene = 570. Reaction temperatures were as follows: [c] −47°, [d] −22°, [e] 1–4°, [f] 2°.

Thus, *trans*-3-hexene, which has two ethyl groups on the double bond, reacts about 11 times faster than 1-hexene, which has only one alkyl group on the double bond. 2,3-Dimethyl-2-butene (tetrasubstituted) reacts about six times as fast as *trans*-3-hexene. Unsymmetrical, disubstituted 2-methyl-1-pentene can stabilize a positive charge more readily than *trans*-3-hexene can and reacts about twice as fast.

Like *trans*-3-hexene, the five cyclic olefins are all disubstituted olefins but the relative reactivity for the slowest, cyclooctene, is only about one-twelfth that of the fastest, norbornene, and all are less reactive than *trans*-3-hexene.

The reactivity range from the slowest to the fastest in the cyclic and acyclic, disubstituted internal olefins is a factor of about 16. The major cause of this large spread appears to be complexation with iodine. These complexation phenonema are beyond the scope of the present paper but will be considered in detail in a subsequent article. We will also consider relative reactivities derived from competitive reactions of pairs of olefins with preformed solutions and with *in situ* generated iodine isocyanate. The present paper is concerned only with the relative reactivity encountered in the heterogeneous, *in situ* systems.

Surprisingly, vinyl acetate is almost 40 times as reactive as 1-hexene. The difference must reflect the effect of the acetoxy group compared with the *n*-butyl group. Vinyl acetate, however, is known to react slowly with electrophilic reagents. Hanna and Siggia[10] noted that bromination of vinyl acetate in acetic acid is much slower than that of 1-octene. Vinyl acetate also reacts slowly with iodine monochloride[11] and peroxyacetic acid.[12] These results suggest that the acetoxy group is less electron-donating than is an alkyl group. On the other hand, the acetoxy group is known to be activating in electrophilic aromatic substitution.[13,14]

If electrophilic attack on vinyl acetate is actually involved here, we would expect to observe an additional increase in rate with isopropenyl acetate since it could form the more highly stabilized tertiary carbonium ion. Isopropenyl acetate reacts about twice as fast as vinyl acetate (Table II). We must conclude that the acetoxy group is able to stabilize a positive charge effectively in the enol esters studied.

Alkynes, such as 3-hexyne, react very slowly with iodine isocyanate generated *in situ*. The slowness of this reaction, as compared with similar alkene reactions, may be due to the difficulty of forming the unsaturated iodonium ion, or that iodine adds to the triple bond to form a vinylic diiodide that reacts slowly.

The relative reactivity of iodine isocyanate with unsaturated compounds agrees fairly well with electrophilic reactivity orders shown in the literature but not

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(10) J. G. Hanna and S. Siggia, *Anal. Chem.*, **37**, 690 (1965).

(11) D. Swern and E. F. Jordan, Jr., *J. Amer. Chem. Soc.*, **70**, 2334 (1948).

(12) L. S. Silbert, Z. B. Jacobs, W. E. Palm, J. P. Witnauer, W. S. Port, and D. Swern, *J. Polym. Sci.*, **21**, 161 (1956).

(13) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 430.

(14) L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, p 627.

with the reactivity orders of reagents that react *via* a cyclic or free-radical mechanism. These observations support the conclusion that iodine isocyanate behaves as an electrophilic reagent.

The relative reactivities also show that it is advantageous to use the *in situ* method to prepare iodine isocyanate adducts of internal olefins since the total reaction time (INCO generation plus addition) is less than that required to perform iodine isocyanate and add it to the double bond. With terminal olefins, dienes, or alkynes, the use of performed solutions of iodine isocyanate is the method of choice.[15]

Registry No.—Iodine isocyanate, 3607-48-5; methyl [1-(iodomethyl)heptyl]carbamate, 16666-25-4; 4-iodo-3-aminohexane hydrochloride, 16666-26-5; 3-iodo-2-amino-2,3-dimethylbutane hydrochloride, 16666-27-6.

[15] B. Grimwood and D. Swern, *J. Org. Chem.*, **32**, 3665 (1967).

Some Rate Studies and Their Mechanistic Implications for the Reaction of 2-Methylquinoline 1-Oxide and Acetic Anhydride[1]

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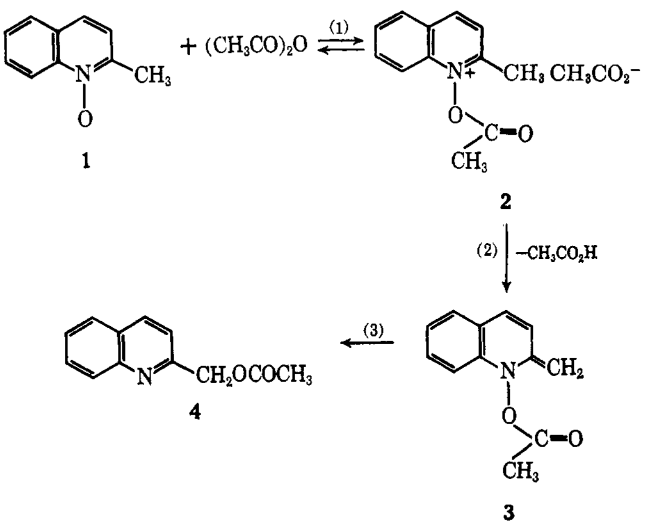
The rate of reaction of 2-methylquinoline 1-oxide (**1**) with acetic anhydride has been measured by three methods which gave similar results. The rate constants are believed to be a product of the equilibrium constant for reaction of **1** with acetic anhydride to form 1-acetoxy-2-methylquinolinium acetate (**2**) and of a rate constant for the latter to yield 2-quinolylmethyl acetate (**4**). α,α,α-Trideuterio-2-methylquinoline 1-oxide was found to react one-half as rapidly as the undeuterated derivative. This, plus the fact the product (**4**) formed at about the same rate as the equilibrium mixture of **1** and **2** disappeared, indicates that removal of a methyl hydrogen is the rate-determining step. Also it can be seen that any intermediate between **2** and **4** must have a very fleeting existence.

The reaction of 2- and 4-alkylaromatic N-oxides has been the subject of many synthetic and mechanistic studies; however, only one report,[3,3a] is available on the reaction kinetics of an alkylaromatic N-oxide, 2-methylquinoline 1-oxide, with acetic anhydride. Kinetic studies have been made on the reaction of pyridine N-oxide[4,5] and of acridine N-oxide[6] with acetic anhydride.

The following is a brief summary of some of the facts about the mechanism of the reaction of 2-alkylaromatic N-oxides and acetic anhydride. The example being cited is 2-methylquinoline 1-oxide (Scheme I) which is known to differ from 2-methylpyridine 1-oxide only in a slower rate of reaction and in more products for the latter. The first step is reversible based on C^{14} labeling and product studies.[7] 1-Acetoxy-2-methylquinolinium perchlorate undergoes reaction with acetate ion, trimethylamine, or cyanide ion to yield **4**.[7] This indicates that it is possible for **2** to be an intermediate in the reaction of **1** with acetic anhydride to yield **4** and also it can be seen from the results of the reactions with trimethylamine and with cyanide that the product (**4**) has the same acetoxy group which **2** had. The reaction of **2** to yield **4** involves scrambling of the oxygens of the acetoxy group as shown by O^{18}-labeling studies.[8] The fact that the reaction of 1-acetoxy-2-(α,α-dideuteriobenzyl)pyridinium perchlorate with sodium acetate when carried to half-completion showed no deuterium decrease in starting material[9] indicates by analogy that any intermediate or product formed after **2** is not in equilibrium with **2**. This implicates the removal of a proton as the rate-determining step. Compound **3**, an anhydro base, is a reasonable intermediate which has often been postulated, but its presence has not been detected.[10]

Scheme I



Much of the recent effort in this area has been to determine whether the N–O bond undergoes homolytic or

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[1] Presented in part before the Division of Organic Chemistry of the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967.

[2] (a) Based in part on the Ph.D. Dissertation, 1964, of R. S. Darlak who was a NDEA Fellow, 1960–1963. This assistance is gratefully acknowledged. (b) Based in part on the Ph.D. Dissertation, 1966, of M. L. DeMatte who had a West Virginia University Senate Research Grant during the summer of 1965. This assistance is also gratefully acknowledged.

[3] S. Furukawa, *Yagkugaku Zasshi*, **79**, 492 (1959); *Chem. Abstr.*, **53**, 18029 (1959).

[3a] Note Added in Proof—See S. Oae, S. Tamagaki, T. Negoro, K. Ogino, and S. Kozuka, *Tetrahedron Lett.*, No. 8, 917 (1968), for a preliminary report on kinetic studies of 2- and 4-alkyl-substituted heteroaromatic N-oxides with acetic anhydride.

[4] J. H. Markgraf, H. B. Brown, S. C. Mohr, and R. G. Peterson, *J. Amer. Chem. Soc.*, **85**, 958 (1963).

[5] S. Oae and S. Kozuka, *Tetrahedron*, **21**, 1972 (1965).

[6] J. H. Markgraf and M.-K. Ahn, *J. Amer. Chem. Soc.*, **86**, 2699 (1964); J. H. Markgraf and C. G. Carson, *J. Org. Chem.*, **29**, 2806 (1964).

[7] C. W. Muth and R. S. Darlak, *ibid.*, **30**, 1909 (1965).

[8] S. Oae, T. Kitao, and Y. Kitaoka, *J. Amer. Chem. Soc.*, **84**, 3359 (1962); S. Oae and S. Kozuka, *Tetrahedron*, **20**, 2671 (1964).

[9] V. J. Traynelis and P. L. Pacini, *J. Amer. Chem. Soc.*, **86**, 4917 (1964).

[10] V. J. Traynelis, private communication. Spectral evidence for an anhydro base in the reaction of 1-acetoxy-4-benzylpyridinium perchlorate with acetate ion has been obtained.