

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA, EDMONTON, ALBERTA, CANADA]

Polar Radicals. I. Succinimide Radicals Generated from N-Iodosuccinimide

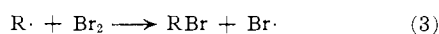
BY DENNIS D. TANNER

RECEIVED MAY 23, 1964

The reactivity and fate of protonated succinimide radicals generated by the photolysis of N-iodosuccinimide in trifluoroacetic acid have been studied. A mechanism, based in part upon the abstraction of a hydrogen atom from trifluoroacetic acid by a protonated succinimide radical, is proposed to explain the light-catalyzed reaction of N-iodosuccinimide in that solvent.

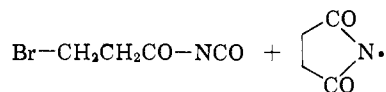
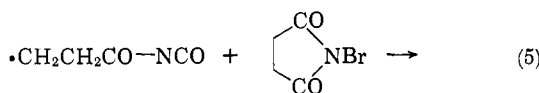
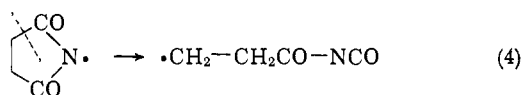
Introduction

Owing to the current interest in N-bromosuccinimide (NBS)¹⁻³ the reactivity or lack of reactivity and the ultimate fate of the succinimide radical have been of some interest to us. Studies of the reactivity of NBS have demonstrated the chain-carrying species for its free-radical bromination reactions to be most likely the bromine atom, and it is proposed that the chain sequence does not involve a succinimide radical (1-3).



This position seems to be supported by the work of Djerassi and Lenk⁴ who showed N-iodosuccinimide (NIS) to be unreactive toward toluene under the conditions normally employed for free-radical halogenation by NBS.

A radical chain reaction involving succinimide radicals has been suggested in the well known β -scission reaction of NBS, but the details of this reaction are as yet obscure.^{5,6} The most plausible explanation for the β -scission rearrangement is the following proposed by Martin and Bartlett.⁵



An example of carbon-to-nitrogen hydrogen transfer can be found in the intramolecular rearrangement of N-haloamines,⁷ the Hofmann-Löffler-Freytag reaction (H-L-F). These compounds undergo free-radical chain decomposition to give rearranged chlorides in the presence of strong acids and are stable to light and other free-radical initiators in the absence of strong acid. The behavior of these N-halides has been rationalized by the mechanism proposed by Wawzonek and Thelan^{8a} and later substantiated by the work of Corey and Hertler^{8b} (eq. 6-8).

(1) C. Walling, A. L. Rieger, and D. D. Tanner, *J. Am. Chem. Soc.*, **85**, 3129 (1963).

(2) G. A. Russell and K. M. Desmond, *ibid.*, **85**, 3139 (1963).

(3) R. E. Pearson and J. C. Martin, *ibid.*, **85**, 3142 (1963).

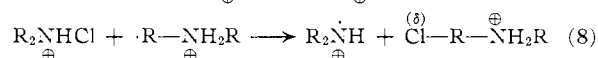
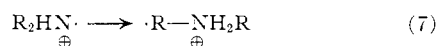
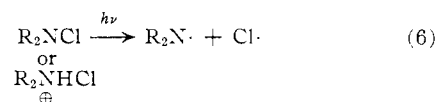
(4) C. Djerassi and C. T. Lenk, *ibid.*, **75**, 3494 (1953).

(5) J. C. Martin and P. D. Bartlett, *ibid.*, **79**, 2533 (1957).

(6) H. W. Johnson, Jr., and D. E. Bublitz, *ibid.*, **79**, 753 (1957); **80**, 3150 (1958).

(7) M. E. Wolff, *Chem. Rev.*, **63**, 55 (1963).

(8) (a) S. Wawzonek and P. J. Thelan, *J. Am. Chem. Soc.*, **72**, 2118 (1950); (b) E. J. Corey and W. R. Hertler, *ibid.*, **82**, 1657 (1960).



Corey and Hertler^{8b} have proposed that catalysis of the H-L-F reaction by strong acid was attributed to the decrease in the rate of bimolecular termination of the protonated radicals involved in the chain and/or to the fact that abstraction by a protonated species was a more favorable reaction than the one in which non-charged radicals were involved.

To examine further the above proposal, and because of our stated interest in N-halosuccinimide and the question of the reactivity of succinimide radicals, an investigation of the photolysis of NIS in trifluoroacetic acid has been undertaken.

Results

N.m.r. Studies of NIS in Trifluoroacetic Acid (TFA).—The light-catalyzed reaction of NIS in TFA could be conveniently followed by examination of the n.m.r. spectrum during the course of the photolysis. When samples of NIS (1.5 M) in TFA were degassed in the absence of light and n.m.r. spectra of the solution were quickly taken, only absorptions at -1.31 and 7.12τ were observed and were assigned to the acidic proton of TFA and the methylene protons of N-iodosuccinimide (NIS), respectively.⁹ A sample could be kept in the dark at 50° for several half-lives of the reaction without any observable change in the spectrum of the solution, and after that time the NIS could be recovered from the mixture unchanged. Irradiation of the sample caused precipitation of iodine from the solution and the changes in the n.m.r. spectrum shown (Fig. 1). The band assigned to NIS diminished, and the one assigned to the methylene protons of succinimide (τ 7.23) increased until it accounted for 78% of the total methylene protons. In conjunction with the growth of the peak at τ 7.23, the N-H proton of succinimide at 0.58τ appeared in the ratio of 4:1.¹⁰ The presence and quantity of the succinimide and of the iodine were confirmed by their isolation and characterization. Accompanying the bands associated with NSH was the absorption assigned to three other minor compounds, each showing

(9) The τ -values reported are relative to $\tau(\text{NSH})$ in TFA as determined by the use of an external tetramethylsilane standard. Calibration with the external standard was obtained on the Varian A-60 n.m.r. spectrometer.

(10) N.m.r. studies of a variety of amides in strong acid confirm that protonation occurs on oxygen rather than nitrogen, and that at room temperature exchange is so rapid that the protonation is not observable: T. Birchall and R. J. Gillespie, *Can. J. Chem.*, **41**, 148, 2642 (1963).

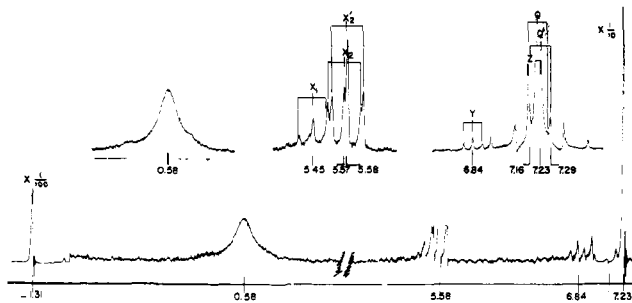


Fig. 1.—N.m.r. spectra of the products of the photolysis of NIS.

an A_2X spectrum. Spin-decoupling experiments showed peaks X_1 and Y to be associated with one compound and peaks X_2 , Q , and X_2' , Q' to be associated with the other two compounds. All three of the minor components were always present in observable amounts, although the compound X_1Y represented only approximately 4% of the total products. When the reaction mixture was fractionated under high vacuum, the liquid fraction contained iodine, TFA, and one of the compounds of the X_2Q pair. When a sample which had been irradiated to completion was placed in a bath thermostated at 90° , the X_2Q and $X_2'Q'$ bands diminished and the X_1Y peaks grew in size.

The reaction was followed by integration of the n.m.r. intensities, and a plot of the mole fraction of the reaction, N_x , vs. the time the sample was irradiated is shown in Fig. 2. It can be seen from Fig. 2 that the rate of formation of NSH begins to approach the rate of formation of the minor X_1Y , X_2Q , and $X_2'Q'$ products, and that by the time the reaction is complete, 22% of the reaction has gone through the minor products.

Another compound, denoted by the singlet Z peak, 7.16τ , is also formed during the photochemical reaction and accounts for 2% of the products found. The amount of the compound found depends upon the amount of trifluoroacetic anhydride present in the trifluoroacetic acid and therefore is presumed to be a product of the reaction of the anhydride and a succinimide radical. By integration of the mixture before and after the completion of the reaction, a material balance could be obtained for all protons observed (reproducible to $\pm 2\%$). Thus we were assured that any compounds not accounted for either contained no hydrogen, had proton chemical shifts which were identical with the absorptions assigned, or were in such minor amounts that they were not readily distinguishable. Traces of compounds having proton absorptions were observable at the low-field side of the X peaks and in the region between $7-7.5 \tau$, but owing to their quantities and absorption frequencies no detailed information could be obtained from their spectra.

The absence of N,N' -bisuccinimidyl was confirmed in all of the experiments reported in this study, and the stability of N,N' -bisuccinimidyl under the reaction conditions was established.

Analysis of Gaseous Products.—Upon opening of the reaction vessels, a copious amount of gas was found to have been formed. The composition of the gas was determined by vapor phase chromatography and mass spectrometry to be $>97\%$ CO_2 and CF_3I with $<1\%$ CF_3H or C_2F_6 present. The ratio of CF_3I/CO_2 varied depending upon the extent of the utiliza-

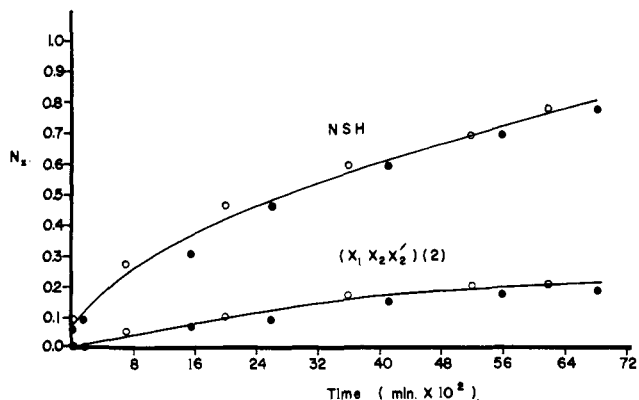


Fig. 2.—Plot of the formation of NSH and R_x vs. irradiation time (open and closed circles are separate reactions).

tion of NIS (Table I). It can be seen (Table I) that the ratio of CF_3I/CO_2 decreases as the reaction proceeds, and although the quantity of gas evolved increases, as expected, the absolute amount of CF_3I produced increases rapidly in the beginning and then begins to slow down. The mole fraction of "excess" CO_2 could be calculated, if one assumed an initial reaction in which CO_2 and CF_3I are produced in a ratio of one to one, and a competing reaction involving the production of only CO_2 . When this quantity (N_{CO_2}) was compared with the mole fraction of the minor products X_1Y , X_2Q , and $X_2'Q'$ produced (N_i), an extremely good correlation was observed (Table I).

TABLE I
ANALYSIS OF THE PRODUCTS OF PHOTOLYSIS OF NIS
(15.0×10^{-4} MOLE)

Reaction, %	CF_3I , moles $\times 10^4$	CO_2 , moles $\times 10^4$	CF_3I/CO_2	N_{CO_2} (excess)	N_i
17	0.35	0.51	0.71	0.01	0.01
36	1.14	1.94	.59	.05	.05
59	1.86	3.01	.62	.08	.09
65	2.22	3.73	.59	.10	.12
68	1.95	3.42	.56	.10	.12
70	1.97	3.53	.57	.10	.08
70	1.79	3.59	.50	.12	.13
89	2.25	4.56	.49	.15	.14
98	2.42	4.86	.50	.16	.20
100	1.61	5.17	.32	.24	.22

Thiosulfate determination of the iodine produced at 100% reaction plus the iodine contained in CF_3I established that 99% of the iodine can be accounted for in these two products.

Substitution of Cyclohexane by NIS.—The photolysis of NIS in trifluoroacetic acid with added cyclohexane proceeded, qualitatively at least, much more rapidly than the reaction without the added hydrocarbon, although the cyclohexane was only slightly soluble in the mixture. Analysis of the gaseous products ($>97\%$ CO_2 and CF_3I) showed that much less CO_2 and CF_3I were produced in runs with added cyclohexane than without, and that at 100% reaction of NIS only half the amount of the minor products (X_1Y , X_2Q , and $X_2'Q'$) were produced. Fractionation of the reaction mixture by vapor phase chromatography showed the major product peak to have an identical retention time with that of the trifluoroacetate of cyclohexanol. The n.m.r. spectrum of cyclohexyl trifluoroacetate is consistent with the new peaks ob-

served in the reaction mixture, although the spectrum could not be completely resolved.

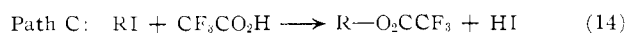
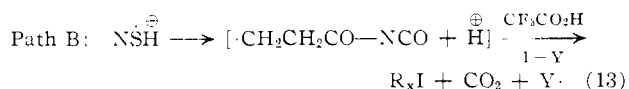
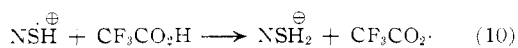
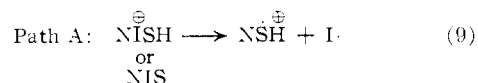
Table II shows an example of the yields obtained for the complete photolysis of NIS in trifluoroacetic acid with and without added cyclohexane.

TABLE II
YIELDS OBTAINED FROM THE PHOTOLYSIS OF 15.0×10^{-4}
MOLE OF NIS WITHOUT, 1, AND WITH, 2, ADDED CYCLOHEXANE

	NSH, moles $\times 10^4$	A ₂ X ₂ , moles $\times 10^4$	CO ₂ , moles $\times 10^4$	CF ₃ I, moles $\times 10^4$	I ₂ , moles $\times 10^4$
1	11.7	3.3	5.17	1.61	6.7
2	13.4	1.6	3.23	1.21	

Discussion

The production of succinimide (NSH) during the photolysis of NIS implies that a hydrogen is supplied either by trifluoroacetic acid or by NIS itself. Since all of the products which were present in assignable amounts, as determined by n.m.r., were found to consist either of succinimide or of compounds having two nonequivalent pairs of methylene protons, the predominant hydrogen source for succinimide production is the acidic proton of trifluoroacetic acid. Since the reaction did not proceed at an observable rate in the absence of light, even at 50°, a mechanism involving free-radical intermediates is considered mandatory.



The pathways depicted above satisfactorily account for the production of all of the products that have been identified. Reactions 9-12 account for approximately 20% of the reaction if the extent of the abstraction from trifluoroacetic acid can be estimated by the amount of trifluoromethyl iodide formed during the reaction, on the assumption that no trifluoroacetoxy or trifluoromethyl radicals reacted in a manner other than to give trifluoromethyl iodide and carbon dioxide. Reactions 9-12 may form a chain sequence depending upon whether (-Y) is equal to succinimide or iodine. Since the NIS is only in a mole ratio of 1:10 compared with the trifluoroacetic acid, it is not surprising that some trace products are detectable. The fact that abstraction products from succinimide are not clearly observed indicates the abstracting species, the protonated succinimide radical, to be an extremely reactive and nonselective radical.¹¹

Secondary photolytic reactions of trifluoromethyl iodide¹³ or abstraction reactions of trifluoromethyl

(11) The high energy required for abstraction of the acidic proton in carboxylic acids has been calculated by Jaffe, *et al.*^{12a} Abstraction of the proton from TFA has been observed by Szwarc and Smid and is considered by these authors to be an energetically unfavorable process.^{12b}

(12) (a) L. Jaffe, E. J. Prosen, and M. Szwarc, *J. Chem. Phys.*, **27**, 416 (1957); (b) M. Szwarc and J. Smid, *ibid.*, **27**, 421 (1957).

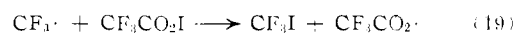
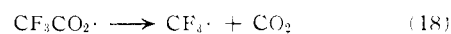
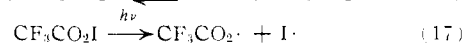
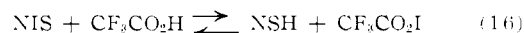
radicals would be expected to yield hexafluoroethane and trifluoromethane. These compounds were not detected in any of the experiments undertaken in this work.

Path B represents the β-scission reaction of NIS. The intermediate radical reacts with iodine or in a chain sequence with NIS. The transient β-propionyl isocyanate radical undergoes subsequent reactions with trifluoroacetic acid and iodine to yield the three products designated X₁Y, X₂Q, and X₂'Q'. Since there is such an excellent correlation between the rearranged products and the "excess" carbon dioxide, one is forced to conclude that reactions of the intermediate isocyanate with trifluoroacetic acid yield also a molecule of carbon dioxide.

Since 99% of the iodine could be accounted for as molecular iodine or trifluoromethyl iodide, it must be assumed that the rearrangement products (22% of the reaction product) have undergone further solvolytic reaction with the trifluoroacetic acid and that the hydriodic acid produced has reacted with unreacted NIS (eq. 14-15). In this case the solvolysis reaction must be faster than the photoinitiated reaction of NIS. In fact, only a maximum value of 5% of the products found, exclusive of trifluoromethyl iodide, can contain iodine, and any solvolysis to form HI must have taken place before the depletion of the NIS.

An indication that β-iodopropionyl isocyanate was indeed the intermediate leading to formation of the A₂X₂ compounds in trifluoroacetic acid was obtained by treating β-bromopropionyl isocyanate¹⁴ with that solvent. On mixing the reactants, an exothermic reaction with the liberation of a gaseous product was observed. The gas was identified as CO₂ by its precipitation as barium carbonate. The reaction mixture was heated at 90° and the appearance in the n.m.r. of a compound having a spectrum identical with that of the X₁Y compound was observed.¹⁴

The possibility of an ionic equilibrium existing between NIS and trifluoroacetic acid in lieu of path A has been investigated. The inference is that the photo-induced decomposition involved trifluoroacetyl hypoiodite and not NIS. The hypoiodite would have to have the added restriction that it was thermally stable at 50° under the reaction conditions.

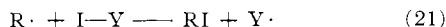
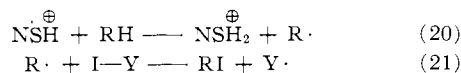


In contrast to the mechanism depicted by eq. 9-12, the above sequence of reactions can account for the formation of trifluoromethyl iodide and carbon dioxide without the involvement of a hydrogen abstraction reaction. The substitution of a hydrocarbon having abstractable hydrogen, such as cyclohexane, clearly demonstrates that radical abstraction has taken place. Since a limited number of radicals in the system can be postulated, the species responsible for the abstraction of hydrogen from trifluoroacetic acid and/or cyclohexane can be established. The

(13) J. R. Dacey, *Discussions Faraday Soc.*, **14**, 81 (1953).

(14) The nature of the β-scission reaction and the rearranged products obtained in trifluoroacetic acid is currently under investigation and the results of this work will be published elsewhere.

inability of iodine to abstract hydrogen at ordinary temperatures is well established,¹⁵⁻¹⁷ and with the absence of trifluoromethane in the gaseous products, the participation of trifluoromethyl radical can also be discounted as the abstracting species. The possibility that trifluoroacetoxy radicals might be responsible for the abstraction of hydrogen in the reaction with added cyclohexane is highly unlikely since the well established nonreactivity of acetoxy and substituted acetoxy radicals toward transfer reactions is well documented.^{18,18-20} The abstracting species is therefore suggested to be the protonated succinimide radical (eq. 9-12, 20-21).



That cyclohexane competes effectively with trifluoroacetic acid for succinimide radicals, even though the hydrocarbon was only slightly soluble, has been demonstrated by the reduction of the quantity of trifluoromethyl iodide and carbon dioxide produced during the competition reaction. The high percentage of β -scission products produced in trifluoroacetic acid may be attributed to the poor chain-transfer properties of the carboxylic acid, but in the presence of the hydrocarbon the amount of rearrangement observed was substantially reduced.

In NBS reactions in nonprotonating solvents, the reactivity of succinimide radicals is either identical with that of the bromine atom toward hydrogen abstraction, or it is so poor a competitor that the succinimide chain is virtually nonexistent. In a protonating solvent, trifluoroacetic acid, the reactivity of the succinimide radical is enhanced to the extent that abstraction from trifluoroacetic acid becomes a favorable reaction, a process that is energetically not available during the reaction of bromine atoms in acetic acid.^{21,22}

A quantitative investigation of the energetics of polar radicals in other systems is now under way in this laboratory.

Experimental

Materials.—Trifluoroacetic acid and trifluoroacetic anhydride were Eastman White Label chemicals. Before use they were distilled, and their purity was checked by g.l.c. and n.m.r. Cyclohexane was Phillips research grade hydrocarbon. N-Iodosuccinimide used was either prepared by the method of McBee and Benson²³ or was commercially available material. The purity of the NIS, m.p. 199–201°, was checked by iodometric titration, 100.6–101.0%.²⁴ Different batches of NIS gave identical results. N,N'-Bisuccinimidyl was prepared as suggested by Hedaya and co-workers,²⁵ using the method of Feuer and Wynn²⁶;

(15) J. M. Tedder, *Quart. Rev.* (London), **14**, 336 (1960).

(16) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957.

(17) The possible enhancement of the reactivity of iodine atoms by protonation, allowing them to function as the abstracting species, was considered. Photolysis of an iodine-saturated solution of trifluoroacetic acid and also a solution with added cyclohexane gave no detectable reaction products when the photolysis was carried out to greater than two half-lives for the NIS reaction.

(18) A. Fry, B. N. Tolbert, and M. Calvin, *Trans. Faraday Soc.*, **49**, 1444 (1953).

(19) M. Levy and M. Szwarc, *J. Am. Chem. Soc.*, **76**, 5983 (1954).

(20) M. Szwarc, "Peroxide Reaction Mechanisms," Interscience Publishers, Inc., New York, N. Y., 1960.

(21) M. S. Kharasch and F. R. Mayo, *J. Am. Chem. Soc.*, **55**, 2468 (1933).

(22) M. S. Kharasch, P. C. White, and F. R. Mayo, *J. Org. Chem.*, **3**, 33 (1938).

(23) E. T. McBee and W. Benson, *Org. Syn.*, **43**, 73 (1963).

(24) T. Waugh "NBS, Its Reactions and Uses," Arapahoe Chemicals, Inc., 1951.

(25) E. Hedaya, R. L. Hinman, and S. Theodoropoulos, *J. Am. Chem. Soc.*, **85**, 3052 (1963).

m.p. 310–311°. *Anal.* Calcd. for C₄H₄O₂N: N, 14.28. Found: N, 14.04. The n.m.r. spectrum in trifluoroacetic acid showed a singlet at 7.13 τ and could be clearly separated from the absorption of NIS at 7.12 τ .

Photolysis of NIS.—The reactions were carried out in Pyrex, n.m.r. tubes, break seals, or ampoules, depending upon the experimental method used. In the appropriate container was placed the NIS and in the absence of light was added enough trifluoroacetic acid, containing 2% added trifluoroacetic anhydride, to make a 1.5 M solution. The reaction vessels were vacuum degassed, and the samples were irradiated with a Hanovia high pressure mercury lamp. The reactions were carried out at ambient temperatures, approximately 30–40°.

N.m.r. Analysis.—The n.m.r. spectra were taken on the Varian HR-100 spectrometer, and the relative areas of the absorption bands were obtained using a Varian V-3521 integrator.

Analysis of Gaseous Products.—In the absence of light, a sample of NIS, 1.5×10^{-3} mole, in 1 ml. of trifluoroacetic acid (2% added anhydride) was degassed and sealed in a Pyrex break seal. The sample was irradiated for the desired length of time. The tube was then opened and the gaseous products formed were distilled under vacuum through a trap cooled by a carbon disulfide freezing mixture, -111° , and collected at liquid nitrogen temperatures. The absolute quantity of the gas was then measured. The gas was subjected to g.l.c. analysis on a 28-ft. dibutyl maleate column, 20% on firebrick. The gas was found to contain two major products which accounted for >97% of the gas. The products were identified as trifluoromethyl iodide and carbon dioxide by mass spectral analysis. A quantitative determination of the percentage composition of the gaseous products was obtained by mass spectral analysis (see Table I). The nongaseous products, the products not passing the -111° trap, were analyzed by n.m.r. spectra to determine the extent of the reaction.

Isolation of Succinimide and Iodine.—The reaction mixture, at the completion of the reaction, was cooled and the mixture decanted from the precipitated iodine. The iodine was air dried, weighed, and titrated with thiosulfate. Alternatively, the reaction mixture was diluted with water, and the iodine present was determined directly by thiosulfate titration.²⁴ The iodine determined by titration and/or isolated, 83%, and the iodine present as trifluoromethyl iodide, 16%, comprised 99% of the theoretical iodine. The solution was vacuum distilled, and the residual oil was dissolved in chloroform and subjected to chromatographic separation on an acid-washed alumina column packed in carbon tetrachloride. The column was eluted with chloroform; 68% of the theoretical amount of succinimide was recovered. The melting point, mixture melting point, and n.m.r. spectrum confirmed its identification.

Abstraction from Cyclohexane.—The reactions and analysis were carried out as before, except that the mixture was made 1.0 M in cyclohexane. The cyclohexane was not completely miscible with the trifluoroacetic acid. Upon irradiation, the reaction proceeded approximately 2.5 times faster than the reaction without added cyclohexane. The n.m.r. spectrum showed absorption corresponding to cyclohexyl trifluoroacetate, but the complete spectrum of the substituted cyclohexane could not be resolved. When the mixture was subjected to g.l.c. analysis on an 8-ft. silicone column, the chromatogram showed the major low boiling product to have a retention time identical with an authentic sample of cyclohexyl trifluoroacetate.²⁷ The reaction products were analyzed. Analysis by g.l.c. of the gaseous products

Reaction, %	CF ₃ I/CO ₂	Rearrangement, %
39	0.33	~2
100	0.27	11

showed <0.3% of CF₃H. It could be estimated from the n.m.r. spectrum of the reaction carried out to 39%, by comparison of the integral of the tertiary hydrogen of the substituted cyclohexane to the NH hydrogen of succinimide, that 40% of the succinimide came from hydrogen abstraction from cyclohexane.

Acknowledgment.—The author is indebted to Mr. G. Bigam for operation of the n.m.r. spectrometer and to Dr. J. S. Martin and Mr. G. Bigam for their helpful discussion concerning the spectral results.

(26) H. Feuer and J. E. Wynn, *Chem. Ind.* (London), 577 (1956).

(27) E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, *J. Chem. Soc.*, 3268 (1958).