The Acetylation of Butane 2-Diazotate. Mechanism of Decomposition of an Alkyl Diazo Ester[1,2]

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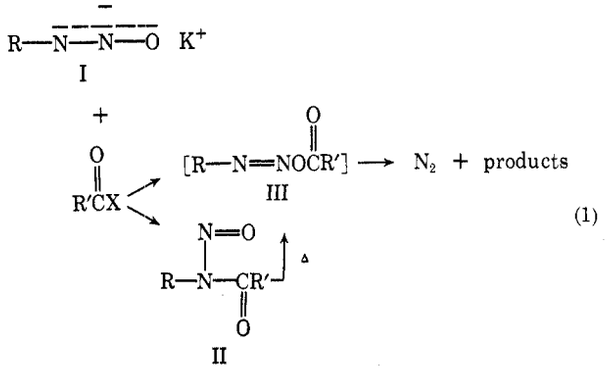
Received August 17, 1971

sec-Butyl acetate is formed with 18–25% net retention in the ethereal thermolysis of *N*-nitroso-*N*-*sec*-butylacetamide. In contrast, acetylation of ethereal butane 2-diazotate, with either acetic anhydride or acetyl chloride, leads to the same ester with 17–21% net inversion. The stereochemical responses of both reactions to changes in reaction conditions are examined, and it is concluded that the heterogeneity of the diazotate reaction is responsible for its unique behavior.

Due to the ambident character[4] of alkane diazotate salts I, their acylation affords *N*-alkyl-*N*-nitrosoamides II and the unstable alkyl diazo esters III (eq 1). In-

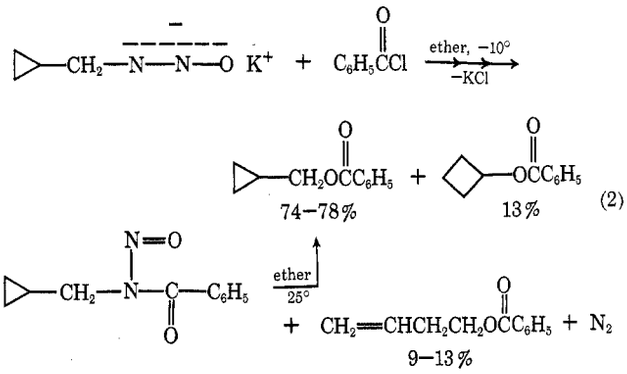


(1)

termediates III are well known in the thermal rearrangements of independently prepared II.[5,6]

Indeed, there are several studies of reaction 1, and these suggest that the partition between products II and III is quite sensitive to the identity of R. When R = CH_3, N-acylation (formation of II) is a major pathway.[4] When R = 2,2-diphenyl-1-cyclopropyl, O-acylation is the sole detected pathway; steric hindrance toward N-acylation by the bulky R group was cited as the probable cause of this path reversal.[7]

Not surprisingly, with a primary substituent in I, R = cyclopropylcarbinyl, we were able to observe both N-acylation (10%) and O-acylation in the reaction of I with benzoyl chloride.[8] More importantly, as summarized in eq 2, the product distribution obtained upon benzoylation of the diazotate was nearly identical with that observed in a separate thermolysis of *N*-cyclopropylcarbinyl-*N*-nitrosobenzamide. It appeared that



(2)

the product-determining steps were the same for both reactions, and (perhaps less cogently) that both reactions involved the identical penultimate precursor, cyclopropylcarbinyl diazobenzoate.[8]

We have now studied the acetylation of butane 2-diazotate and the thermolysis of *N*-nitroso-*N*-*sec*-butylacetamide. The starting materials were optically active, and the stereochemical courses of formation of *sec*-butyl acetate were compared as a test for identity of mechanism.

In contrast to the earlier examples,[8] we find important differences in the present reactions. The results implicate SN2-type reactions of *sec*-butyl diazo acetate, following the acetylation of the diazotate, and they may have meaningful consequences for deamination chemistry[6] and for the chemistry of alkane diazotates.

Results

The Acetylation Reaction.—By an unexceptional sequence of reactions, 2-aminobutane was converted through *N*-2-butylurethan and *N*-nitroso-*N*-2-butylurethan to potassium butane 2-diazotate.[9-11] In the initial acetylation studies, either acetyl chloride (AcCl) or acetic anhydride (Ac_2O) in dry ether was rapidly added to the suspended ethereal diazotate at about −19°. Because 2 equiv of *tert*-butoxide are used in the cleavage of the *N*-nitrosourethan to the diazotate,[9] 2 equiv of acetylating agent were added in the decomposition step, sufficient to acetylate both the excess *tert*-butoxide and the diazotate.

Nitrogen evolution (80–100%) was complete in about 3 min, and an aqueous work-up, followed by gas chromatography (gc), allowed the isolation and identification

(1) Alkyl Diazotates. Part X.

(2) Part IX: R. A. Moss, A. W. Fritz, and E. M. Emery, *J. Org. Chem.*, **36**, 3881 (1971).

(3) Fellow of the Alfred P. Sloan Foundation.

(4) Bond orders of ~1.5 have been established for the N–N and N–O bonds of I, R = CH_3: E. Müller, W. Hoppe, H. Hagenmaier, H. Haiss, R. Huber, W. Rundel, and H. Suhr, *Chem. Ber.*, **96**, 1712 (1963).

(5) (a) E. H. White, *J. Amer. Chem. Soc.*, **76**, 4497 (1954); (b) E. H. White, *ibid.*, **77**, 6008 (1955); (c) **77**, 6011 (1955); (d) **77**, 6014 (1955); (e) R. Huisgen and H. Reimlinger, *Justus Liebigs Ann. Chem.*, **599**, 161 (1956); (f) R. Huisgen and C. Rüchardt, *ibid.*, **601**, 1 (1956), and earlier references in this series.

(6) Recent reviews, which cover various aspects of deamination chemistry, include (a) E. H. White and D. J. Woodcock in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, New York, N. Y., 1968, pp 440–483; (b) J. T. Keating and P. S. Skell, in "Carbonium Ions," II, G. A. Olah and P. v. R. Schleyer, Ed., Wiley–Interscience, New York, N. Y., 1970, p 573 ff; (c) L. Friedman, *ibid.*, p 655 ff; (d) R. A. Moss, *Chem. Eng. News*, **49** (48), 28 (1971).

(7) T. K. Tandy, Jr., and W. M. Jones, *J. Org. Chem.*, **30**, 4257 (1965).

(8) R. A. Moss and F. C. Shulman, *Tetrahedron*, **24**, 2881 (1968).

(9) R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).

(10) R. A. Moss and G. H. Temme, III, *Tetrahedron Lett.*, 3219 (1968).

(11) See the Experimental Section for details.

TABLE I

STEREOCHEMISTRY OF FORMATION OF *sec*-BUTYL ACETATE IN THE ACETYLATION OF BUTANE 2-DIAZOTATE

Run	Diazotate[a]	Decomposing reagent	Mode of addition	N_2 evolved,[b] %	α_D for *sec*-BuOAc,[c] deg	α_D corrected,[d] deg	Stereochemistry, %[e]
1	13.2 mmol in 40 ml of ether[f]	Ac_2O, 26.4 mmol in 25 ml of ether	Direct[g]	90	$\alpha^{23}D$ −0.462[h]	−3.62	16.6 net inv
2	13.8 mmol in 35 ml of ether[f]	Ac_2O, 27.6 mmol in 25 ml of ether	Direct[g]	92	$\alpha^{26}D$ −1.121[i]	−4.26	19.9 net inv
3	17.2 mmol in 47 ml of ether[j]	AcCl, 35 mmol in 13 ml of ether	Direct[g]	100	$\alpha^{22}D$ −0.849[k]	−3.84	17.6 net inv
4	17.2 mmol in 30 ml of ether[j]	AcCl, 35 mmol in 15 ml of ether	Direct[g]	90	$\alpha^{22}D$ −1.889	−4.65	21.2 net inv
5	17.2 mmol in 35 ml of ether[j]	AcCl, 35 mmol in 25 ml of ether	Inverse[l]	*m*	$\alpha^{22}D$ −0.549[n]	−4.76	21.8 net inv
6	17.2 mmol in 55 ml of CH_2Cl_2 +49.2 mmol of dry C_2H_5OH[j]	AcCl, 74 mmol in 250 ml of ether	Inverse[o]	86	$\alpha^{23}D$ +0.223[p]	+1.21	5.53 net ret
7	17.2 mmol in 40 ml of CH_2Cl_2 +51 mmol of dry C_2H_5OH	AcCl, 86 mmol in 500 ml of ether	Inverse[o]	109	$\alpha^{23}D$ −0.017[q]	0.0	Racemization
8	17.2 mmol in 35 ml of HMPA[r]	AcCl, 38.5 mmol in 250 ml of ether	Inverse[s]	89	$\alpha^{20}D$ −1.29[t]	−6.71	30.1 net inv
9	17.2 mmol in 45 ml of HMPA[r] +86 mmol of NaOAc	Ac_2O, 36.8 mmol in 5 ml of HMPA	Direct[u]	*m*	$\alpha^{18}D$ −0.419[v]	−9.53	42.7 net inv

[a] The ether used in all runs was dried over molecular sieves prior to use; 1 equiv of excess $K^+{}^-O$-*tert*-Bu was present. The reaction temperature varied from ~25 to 35°. [b] Nitrogen was determined manometrically; butenes were removed by a sulfuric acid scrubber. [c] All readings were taken in a 0.5-dm cell on neat ester; zero readings were made on racemic ester. A minimum of 10 readings were made for each sample, and the (average) final reading is considered accurate to ±0.02°. This implies a per cent error of ±10% in the stereochemistry of run 6. The per cent error in the other runs is considerably smaller. [d] Corrected for path length, for dilution, and for the optical purity of the initial urethan. [e] Optically pure *d*-*sec*-butyl acetate has $\alpha^{20}D$ +22.30 and $\alpha^{27}D$ +21.38; see ref 17. α_D varies linearly with temperature in this range,[17] and $\alpha^{23.5}D$ +21.84° can be interpolated. In a given run, the most appropriate of these values is used. [f] The *N*-2-butylurethan, from which the diazotate derived, had $\alpha^{23}D$ +15.58° corresponding to an optical purity of 85.6%.[14] [g] The acetylating agent was added to the suspended diazotate. [h] 31.8 mg of product acetate was diluted with 74.9 mg of racemic acetate; *i.e.*, the dilution factor was 1067/318. [i] Dilution factor, 1151/710. [j] The *N*-2-butylurethan precursor had $\alpha^{22}D$ +14.78°, corresponding to an optical purity of 81.2%.[14] [k] Dilution factor, 1223/666. [l] The diazotate slurry was added to the acetylating agent over a period of 30 min. The reaction mixture was mechanically stirred in a Morton flask, and the entire reaction was carried out in a dry-box. [m] Not determined. [n] Dilution factor, 1169/332. [o] The diazotate was in the form of a colloidal suspension. It was stable to small quantities of ethanol (~1 equiv) in CH_2Cl_2.[18] The suspension was added to the rapidly stirred AcCl solution. [p] Dilution factor, 1196/545. [q] This value is within the reading error, and is taken as 0.00. It was determined on *undiluted* product ester. [r] HMPA = hexamethylphosphoric triamide. The diazotate was prepared from *N*-2-butylurethan ($\alpha^{21}D$ +17.37°) of 95.45% optical purity.[14] [s] The diazotate was in the form of a clear purple solution. [t] Dilution factor, 1173/473. [u] The acetylating reagent was added to the diazotate solution, which contained excess (solid) sodium acetate. Not all of the diazotate was in solution. [v] Dilution factor, 975/90.

of *sec*-butyl acetate in yields ranging from 14.5 (AcCl reaction)[12] to 23.4% (Ac_2O reaction).

We also observed substantial olefin yields in these reactions. In the Ac_2O reaction, 45% of a butene mixture (determined gravimetrically as the dibromides) was isolated by low-temperature distillation, and shown by direct gc analysis[11] to consist of 1-butene, *trans*-butene, and *cis*-butene in the distribution 68:21:11. From an AcCl reaction, also at −19°, the same olefins were obtained in a 67:21:12 distribution. (A minor gc component with a retention time intermediate between that of *trans*- and *cis*-butene could have been methylcyclopropane.)

In contrast to our results with the primary diazotate, eq 2,[8] no *N*-*sec*-butyl-*N*-nitrosoacetamide was detected in the product mixture resulting from the acetylation of butane 2-diazotate; the crude product mixtures did not evolve nitrogen on standing.

Qualitative and preparative gc of the crude product mixtures revealed the presence of *tert*-butyl alcohol, *sec*-butyl alcohol, *tert*-butyl acetate, acetic acid, diethyl carbonate, ethyl *tert*-butyl carbonate, ethyl *sec*-butyl carbonate, di-*tert*-butyl carbonate, *sec*-butyl-*tert*-butyl carbonate, and *N*-2-butylurethan. A digression into the probable origins of these mechanistically peripheral products seems in order here.

The diazotate is generated in the presence of excess potassium *tert*-butoxide.[9] Under these conditions, the initial by-product, ethyl *tert*-butyl carbonate, undergoes transesterification reactions leading to diethyl and di-*tert*-butyl carbonates.[9] As demonstrated separately, *sec*-butyl acetate, potassium *tert*-butoxide, and diethyl carbonate, in ether, give rise to carbonates containing the *sec*-butyl moiety. We believe that the traces of such carbonates observed in the diazotate acylation reactions arise during the acetylation step, from product *sec*-butyl acetate.

The small amount of 2-butanol observed (<5%) may have come either from *sec*-butoxide liberated during the transesterifications which accompany the acetylation of the diazotate, or from a minor hydrolysis of *sec*-butyl acetate during the work-up. The trace of *N*-2-butylurethan probably came from butoxide-induced denitrosation of the *N*-nitroso-*N*-2-butylurethan, during the generation of the diazotate. Nmr spectra of starting material showed no evidence of unreacted *N*-

(12) The yields are based on *N*-nitroso-*N*-2-butylurethan. In the AcCl reaction, 6.5% of *sec*-butyl chloride was also formed.

TABLE II

STEREOCHEMISTRY OF FORMATION OF *sec*-BUTYL ACETATE IN THE THERMOLYSIS OF *N*-NITROSO-*N*-*sec*-BUTYLACETAMIDE

Run	Conditions[a]	α_D for *sec*-BuOAc,[b] deg	α_D corrected,[c] deg	Stereochemistry, %[d]
1	10 mmol of nitrosoamide in 45 ml of ether	$\alpha^{25}D$ +0.919[e]	+5.95	27.2 net ret
2	10 mmol of nitrosoamide in 45 ml of ether	$\alpha^{26}D$ +0.770[f]	+3.80	17.8 net ret
3	10 mmol of nitrosoamide in 45 ml of ether	$\alpha^{24}D$ +0.965[g]	+4.26	19.5 net ret
4	10 mmol of nitrosoamide in 52 ml of ether and 50 mmol of HOAc	$\alpha^{24}D$ +1.05[h]	+3.14	14.4 net ret
5	10 mmol of nitrosoamide in 28.7 ml of ether and 6.22 ml of CH_2Cl_2 and 29 mmol of C_2H_5OH	$\alpha^{23}D$ +0.545[i]	+5.29	24.2 net ret[j]

[a] The quantity of *N*-nitrosoamide is based on the amide submitted to the nitrosation reaction, and assumes 100% conversion. This assumption is valid for run 1, in which 6.5 equiv of N_2O_4 were employed in the nitrosation, and 96% of the theoretical N_2 evolution was subsequently observed. In run 3, however, only 1.6 equiv of N_2O_4 were used, and the nitrosation was probably incomplete, as only 47% of the theoretical N_2 evolution was later observed. [b] See Table I, footnote *c*. [c] Corrected for path length, dilution, and for the optical purity of the precursor amide, 95.8% (see above). [d] See Table I, footnote *e*. [e] Dilution factor, 1370/442. [f] Dilution factor, 1237/523. [g] Dilution factor, 1301/616. [h] Dilution factor, 1220/851. [i] Dilution factor, 1183/255. [j] Gc indicated about 4% of minor impurities in the *sec*-butyl acetate used for the polarimetry. Control gc experiments with various *sec*-butyl derivatives (2-butanol, *sec*-butyl ethyl ether) ruled out the possibility that these impurities contained the (chiral) *sec*-butyl moiety.

2-butylurethan, which could have been carried along to the final product mixture.

Stereochemical Studies.—2-Aminobutane was resolved by the procedure of Bruck,[13] and the *d* amine was converted to the corresponding *d* urethane, which served as the basis for the determination of optical purity.[14] The conversion of the optically active urethan to the diazotate and the latter's acetylation were carried out as for the racemic case. *sec*-Butyl acetate was isolated from the reaction mixture by gc, and its purity was established by gc and ir examination. The optical rotation was measured with a Rudolph polarimeter, reading the neat ester (diluted with racemic ester, when necessary) in a 100-μl, 0.5-dm cell.

In a control experiment, *sec*-butyl acetate, $\alpha^{25}D$ −1.25°, was treated with Ac_2O, acetic acid, diethyl carbonate, *tert*-butyl acetate, 1-butene, and potassium acetate in dry ether for 1 hr at 25°. An aqueous work-up, followed by gc isolation, returned *sec*-butyl acetate, $\alpha^{24}D$ −1.31°. The product of interest appears to be optically stable to simulated experimental conditions.

2-Aminobutane, 2-butanol, and *sec*-butyl acetate of the same rotational sign are known to belong to the same optical series.[15] With this information, the experimentally determined optical purities of initial *N*-2-butylurethan and final *sec*-butyl acetate, and the assumption that no loss of optical activity attends any synthetic procedure through the diazotate formation,[16] the stereochemical consequences of the acetylation of butane 2-diazotate were obtained for several reactions. The data appear in Table I, and represent experiments in which acetylating reagent, solvent, and order of reagent addition were varied.

The *N*-Nitrosoamide Reaction.—For comparative purposes, we also examined the formation of *sec*-butyl acetate by the room temperature thermolysis of *N*-nitroso-*N*-*sec*-butylacetamide. This reaction has been extensively studied by White.[19] We obtained 15.5% of *sec*-butyl acetate, together with a substantial yield of 1-butene, *cis*-butene, and *trans*-butene in the distribution 53:33:14. *sec*-Butyl acetate, formed from the *N*-nitrosoamide in the presence of 5 equiv of DOAc, showed no (<2%) incorporation of deuterium,[20] excluding the substantial intermediacy of 2-diazobutane as an ester precursor. White reached a similar conclusion in a closely related study of the decomposition of *N*-nitroso-*N*-*sec*-butylbenzamide in dioxane.[5d]

Stereochemical Studies.—*d*-2-Aminobutane[13] was converted to *N*-*sec*-butylacetamide with acetic anhydride. The purified amide had $[\alpha]^{24}D$ +15.89° ($CHCl_3$, *c* 6.063 × 10^{-2}) and was 95.8% optically pure based on White's extrapolated value of $[\alpha]^{25}D$ +16.6° in $CHCl_3$.[5d]

The labile *N*-nitrosoamide was prepared by nitrosation of the ethereal amide with N_2O_4 in the presence of suspended NaOAc at −10 to 0°. The temperature was kept below 15° during a rapid aqueous work-up.

Dry *N*-nitroso-*N*-*sec*-butylacetamide was decomposed in a stirred ethereal solution at 28–30° until no further nitrogen evolution was observed (15–18 hr.) The optical purity of the gc-isolated *sec*-butyl acetate was determined as previously described, and the results of several experiments are collected in Table II.

Discussion

The Nitrosoamide Reaction.—An abbreviated version of the general mechanism[6a] is given in eq 3, and can be applied to the data of Table II (R = $CH_3\overset{*}{C}HC_2H_5$).[21] In sufficiently polar solvents, such as dioxane or acetic acid, the collapse of V invariably occurs with net retention.[5d,6a]

That retention is not complete has been explained

(13) P. Bruck, I. N. Denton, and A. H. Lamberton, *J. Chem. Soc.*, 921 (1956).

(14) $\alpha^{21}D$ +18.2° for optically pure *d*-*N*-2-butylurethan.[13] However, see the Experimental Section.

(15) See J. A. Mills and W. Klyne in "Progress in Stereochemistry," Vol. 1, W. Klyne, Ed., Academic Press, New York, N. Y., 1954, p 195.

(16) The only step for which this assumption appears at all questionable is the cleavage of the *N*-nitrosourethan to butane 2-diazotate. The reaction of the latter with phenol affords *o*-*sec*-butylphenol with up to 80% net inversion of the *sec*-butyl moiety.[10] Thus there appears to be little, if any, loss of optical purity in the diazotate formation step.

(17) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **T105**, 830 (1914); see especially p 889.

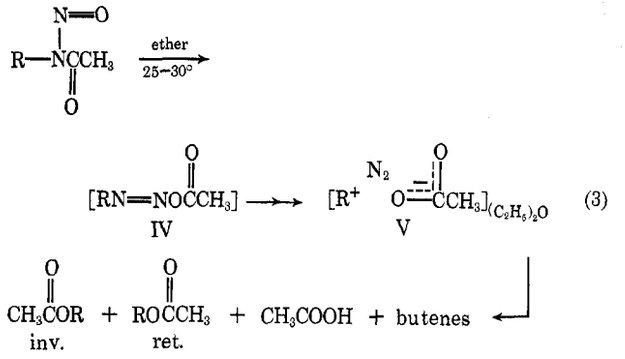
(18) R. A. Moss and M. J. Landon, *J. Amer. Chem. Soc.*, **92**, 5755 (1970).

(19) See especially ref 5d.

(20) Mass spectral analysis employed the ion series *m/e* 86, 87, 88 and 115, 116, 117. See K. Biemann, "Mass Spectrometry: Organic and Chemical Applications," McGraw-Hill, New York, N. Y., 1962, p 225 ff, for a description of the analysis.

(21) It is a matter of some controversy whether a *sec*-carbinyl diazo ester goes to ion pair V with "simultaneous" fission of C–H and N–O bonds, or whether a diazonium carboxylate ion pair ($RN_2^+O^-OCR_t$) is an intermediate. Whiting holds the former view[22] and White, the latter.[6a] The problem is not central in the present context, however.

(22) M. C. Whiting, *Chem. Brit.*, **2**, 482 (1966); H. Maskill, R. M. Southam, and M. C. Whiting, *Chem. Commun.*, 496 (1965).



(3)

by an "intramolecular inversion" mechanism, that is, by the rotation of R^+ within the ion pair, followed by collapse.[6a,23] Some inverted ester could also arise by back-side solvation of V by acetic acid released in prior molecular events; or (less probably) by the annihilation of cations which escaped the initial ion pair.[24]

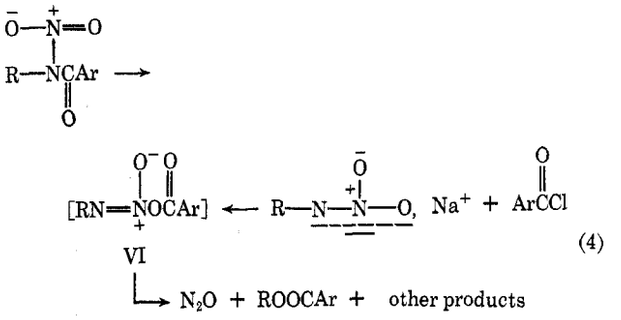
Olefin formation is also a principal fate of V. Not only solvent, but gegenion too acts as a base in the removal of a β proton.[5d,25]

Our ethereal *N*-nitroso-*N*-*sec*-butylacetamide decompositions (Table II) are normal representatives of the general reaction (3). *sec*-Butyl acetate is formed with the anticipated net retention (runs 1–3), and this stereochemical course is only marginally altered in the presence of 5 equiv of acetic acid (run 4), which suggests a limited role for displacement reactions on IV or V. We also observed a 1-butene:*trans*-butene:*cis*-butene distribution of 53:33:14, very similar to that observed by White for a decomposition performed in Na_2CO_3-buffered CCl_4.[5d]

Acetylation of Butane 2-Diazoate.—Formally, this reaction should lead to *sec*-butyl diazoacetate IV, eq 3, the same intermediate involved in the thermolysis of the *N*-nitrosoamide. However, our "calibration" studies of the latter reaction (above), in comparison with the stereochemical data for the acetylation reaction (Table I), prove that there are important mechanistic differences between these reactions.

Differences in mechanism were not expected on the basis of our studies in the cyclopropylcarbinyl system, eq 2.[8] Nor were they anticipated in view of White's related comparative study of the thermal decomposition of (optically active) *N*-nitro-*N*-*sec*-butyl-3,5-dinitrobenzamide and of the reaction of 3,5-dinitrobenzoyl chloride with the sodium salt of *N*-nitro-*sec*-butylamine.[26] *Both* reactions (25°, $CHCl_3$) led to *sec*-butyl 3,5-dinitrobenzoate with about 20% net retention, presumably *via* diazoxy ester VI (eq 4).

We can enumerate the several characteristics which distinguish product formation *via* the acetylation of butane 2-diazotate. (1) *sec*-Butyl acetate is formed with *net inversion* in ethereal decompositions (Table I, runs 1–4). (2) The extent of inversion is independent of the acetylating agent, Ac_2O or AcCl; *i.e.*, the "extra mole" of acetate generated in the Ac_2O reaction is in-



(4)

effective as SN2 nucleophile (runs 1 and 2 *vs.* 3 and 4). (3) The order of reagent addition can be reversed, and hence the average nucleophile and diazo ester concentrations can be altered, without affecting the stereochemistry (run 5 *vs.* runs 1–4). (4) The stereochemical course of the reaction can be changed from inversion to *retention* by changing the solvent system from ether to methylene chloride–ether containing 4 equiv of ethanol (runs 1–5 *vs.* 6 and 7). This is not a bulk solvent effect, because parallel behavior is not observed in the nitrosoamide decompositions (Table II, runs 1–3 *vs.* 5). (5) Acetylation of butane 2-diazotate solubilized in hexamethylphosphoric triamide (HMPA) affords *sec*-butyl acetate with enhanced inversion (Table I, runs 1–4 *vs.* 8 and 9). (6) Relative to other reactions involving the *sec*-butyl cation, the diazotate acetylation yields the most "Hoffmann-like" olefin distribution (Table III).

The inversion in the ethereal diazotate acetylations must result from displacement processes, for the normal stereochemical course of decomposition of ethereal *sec*-BuN=NOAc is retention. In itself, the occurrence of inverting displacement reactions involving such a species is not new. The decomposition of *sec*-BuN=NOOCC$_6$H$_5$ in pentane afforded inverted *sec*-butyl benzoate, which was attributed to inverting attack of benzoic acid (liberated in β-elimination reactions of the diazo ester) on the diazo ester or related species.[5d,21] The extent of inversion was sensitive both to substrate concentration and to the addition of nucleophiles,[5d] as expected for such a process.

We believe that the displacement processes which lead to inverted *sec*-butyl acetate in the diazotate acetylation reactions differ from those identified in the *N*-nitrosoamide decomposition, because the former reaction is stereochemically insensitive to the order of reagent addition, and to the presence of additional acetate during the reaction. The opposite behavior would be expected if the inversion in our reaction had the same origin as that in White's examples.[5d]

Moreover, *ethereal sec*-BuN=NOAc, generated from a *N*-nitrosoamide precursor, is only marginally sensitive to the presence of added acetic acid (Table II, run 4). Again we conclude that the stereochemical variance of the diazotate acetylation cannot be simply explained by an altered substrate/nucleophile ratio, *i.e.*, by a different blend of SN2 and SN1 decompositions of IV.

We suggest that the *heterogeneity* of the diazotate reaction system is responsible for its anomalous stereochemistry. Such inverting processes as 5, or the attack of acetate on the diazo ester, could occur either at the surface of the solid diazotate as it reacts with acetylating agent or, thereafter, in nearby local heter-

(23) E. H. White and C. A. Aufdermarsh, Jr., *J. Amer. Chem. Soc.*, **83**, 1179 (1961).

(24) In dioxane (and presumably in ether) it is likely that solvent oxygen plays a configuration-holding role, through relatively strong back-side solvation of the cation.[6a] This enhances the stereochemical retention in the formation of the product ester.

(25) T. Cohen and A. R. Daniewski, *J. Amer. Chem. Soc.*, **91**, 533 (1969).

(26) E. H. White and D. W. Grisley, Jr., *ibid.*, **83**, 1191 (1961), and references cited therein.

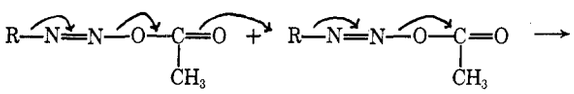
TABLE III

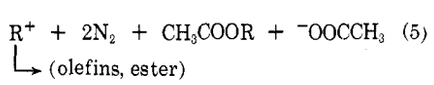
BUTENE DISTRIBUTIONS IN THE DECOMPOSITION OF *sec*-BUTYL X

Case	X	Registry no.	Reaction conditions	% Distribution 1-Butene	*trans*-Butene	*cis*-Butene	Ref
1	OTs	715-11-7	HOAc, 118°	10	47	43	*a*
2	NH_2	13952-84-6	HNO_2, H_2O, 25°	25	56	19	*b*
3	NO | $NCOC_6H_5$	33124-23-1	HOAc, 25°	45	40	15	*c*
4	NO | $NCOC_6H_5$		Dioxane, 25°	49	39	12	*c*
5	NO | $NCOCH_3$		CCl_4, Na_2CO_3, 25°	54	33	13	*c*
6	NO | $NCOCH_3$		Ether, 28°	53	33	14	*d*
7	$N{=}N{-}O^-K^+$		AcCl, Ether, 25°[e]	70	18	12	*d*

[a] Reference 27. [b] Reference 28. [c] Reference 5d. [d] This work. [e] The distributions at −19°, using either AcCl or Ac_2O, are very similar; see above.

ogeneous regions. Such processes would have to be competitive with the rate at which diazo ester escapes into the solvent.[29]





These proposals lead to a consistent, if nevertheless *ad hoc*, interpretation of both present and older data. The inversion and insensitivity to extra acetate and to the order of reagent addition are understandable because, in order to alter the stereochemistry of product formation *via* 5, we would need to change the phase in which the product is formed. Indeed, acetylation of colloidal butane 2-diazotate does produce a marked stereochemical response.[30] (Contrast point 4 with points 1–3, above.) Parity between the diazotate acetylation and the *N*-nitrosoamide thermolysis was not achieved, however, suggesting that some influence of heterogeneity was still operative.

The heterogeneity concept also accommodates recent studies of the $H_2{}^{18}O$ hydrolysis of optically active octane 2-diazotate in ether–water, water, and HMPA–water (solubilized diazotate) systems,[2,31] particularly the observed smooth attenuation of the ^{16}O-conservation–inversion pathway to 2-octanol. It is this pathway which can be most augmented by inverting bimolecular reactions of $RN{=}N^{16}OH$ with itself,[29] and the change in the conservation process stereochemistry, as the solvent system is changed so as to disfavor bimolecular processes (18% net inversion, 22% net retention, and 46% net retention, respectively), is analogous to present results in the *sec*-butyl system.

There are cases in which diazotate decompositions do not exhibit the special characteristics here attributed to heterogeneity effects. Examples include the cylcopropylcarbinyl[8] and *N*-nitro-*sec*-butylamine (sodium salt)[26] systems described above, eq 2 and 4, and the ethanolysis of 1-phenylethane 1-diazotate, which gives 1-phenylethanol (retention) and 1-phenylethyl ethyl ether (inversion).[18] In the latter reaction, the stereochemistries are constant whether ethanol is added to the solid diazotate, or colloidal diazotate (CH_2Cl_2 + 1 equiv of ethanol) or HMPA-solubilized diazotate is added to excess ethanol.

An examination of all the data suggests that poor innate stability of the potential alkyl cation, low solvent polarity, and high gegenion nucleophilicity are experimental factors which accentuate the disparity between the initially heterogeneous diazotate reactions and those homogeneous reactions which formally proceed *via* the same intermediate RN=NX. A more detailed analysis is precluded, in view of the complexities introduced by the heterogeneity.

A final stereochemical point is the enhanced inversion in diazotate acetylation in HMPA (Table I, runs 8 and 9). We believe that SN2 reactions between acetate and *sec*-BuN=NOAc (or related species) are responsible, in these apparently homogeneous, solubilized diazotate reactions.[32] The large nucleophile-potentiating effect of HMPA[33] must enhance the bimolecular component of these decompositions.

A change of the HMPA acetylation procedure from inverse to direct and the addition of excess acetate bring about increased inversion (run 9 *vs.* run 8), but the effect is not large, owing to the low solubility of sodium and potassium acetate in HMPA. Greater inversion might result if a more soluble added nucleophile were employed, and such experiments are planned.

(27) H. C. Brown and I. Moritani, *J. Amer. Chem. Soc.*, **77**, 3607 (1955).

(28) A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **79**, 2888 (1957).

(29) For simplicity, the reactants in eq 5 are shown as covalent species. They might also be rendered as diazonium or carbonium acetate ion pairs. More than two reactants could be linked in such a surface reaction, and the terminal "R^+" could be involved in a concerted proton loss to acetate ion, or could itself be the substrate for an inverting "trigger" attack by acetate, *tert*-butoxide, or even diazotate ion. The last process would give inverted *sec*-butoxide which could be acetylated to product, or appear as 2-butanol after work-up.

(30) In this experiment, we may be dealing with an alcoholate of the diazotate. This could also be an important cause of the altered stereochemistry. The crucial fact, however, is that the stereochemistry of the diazotate reaction changes at all.

(31) R. A. Moss, D. W. Reger, and E. M. Emery, *J. Amer. Chem. Soc.*, **92**, 1366 (1970); R. A. Moss and S. M. Lane, *ibid.*, **89**, 5655 (1967).

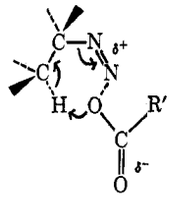
(32) These reactions are probably related to the homogeneous, inverting decompositions described by White.[5d]

(33) For leading references see A. J. Parker, *Chem. Rev.*, **69**, 1 (1969); H. Normant, *Russ. Chem. Rev.*, **39**, 457 (1970); and L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1970, Chapter 8.

Indeed, the present results represent an approach to a synthetically useful SN2 chemistry of amines, which we hope to elaborate.

Elimination Reactions.—β elimination from *sec*-BuN=NOOCR gives more 1-alkene (1-/2-alkene = 0.8–1.2) than does β elimination from either *sec*-BuN_2^+ (1-/2-alkene = 0.33) or from the acetolysis of *sec*-BuOTs (1-/2-alkene = 0.1); see Table III, cases 3–6, 2, and 1, respectively.

The transition state for β elimination from *sec*-BuN=NOOCR has been rendered as VII,[5d] and there is independent evidence for the suggested syn elimination in related cases.[25] Now, it is known that the formation of 1-alkene occurs *via* a sterically less demanding transition state than does that of 2-alkene, since, in competitive situations, the former is augmented by increasing the size of the leaving group, the base, and the β-alkyl group.[34] Though most of this work pertains to E2 eliminations, there appears little reason to doubt that related factors would be operative in controlling the orientation of elimination from VII. VII is a sterically demanding transition state, especially in comparison to that for β elimination from hydrated *sec*-BuN_2^+, and it is therefore not surprising that the butenes from *sec*-BuN=NOOCR are richer in 1-butene. Indeed, VII is related to the transition state for *sec*-butyl acetate pyrolysis, and it is noteworthy that this reaction gives an olefin mixture containing 57% of 1-butene.[35]



VII

The olefin mixture from the acetylation of butane 2-diazotate is even richer in 1-butene than is that from the homogeneous *sec*-BuN=NOOCR decompositions (Table III, case 7 *vs.* cases 3–6). As we rationalized the increased inversion in the substitution reactions, which suceeded the acetylation reaction, by the incursion of a "bimolecular" component, so, too, do we suggest a "bimolecular" component in the accompanying elimination reactions. This component, the products of which are perhaps superimposed on those stemming from competing "unimolecular" elimination *via* VII, must, to satisfy the data, afford an olefin mixture richer in 1-butene than that generated from VII alone.

It is difficult to further specify the nature of the transition state for this "bimolecular" elimination component, because, as in the substitution reactions, ill-defined heterogeneous regions and surface reactions are probably involved. However, it is reasonable that steric constraints in the transition state for such a reaction would be severe, the effective base (alkoxide, acetate, and diazotate ions at the solid surface) would be large, and hence the resulting olefins would be very rich in 1-butene.[36]

Experimental Section

***N*-Nitroso-*N*-*sec*-butylurethan.**—*N*-*sec*-Butylurethan was obtained by the reaction of ethyl chloroformate with 2-aminobutane,[37] and had bp 44–47° (0.2 Torr),[38] infrared (film), 5.87 μ (C=O).[40] The nmr spectrum showed, *inter alia*, 4.05 (q, J = 7 Hz, OCH_2), 3.54 (sextet with additional fine structure, J = 7 Hz, CHN), and 1.20 (t, J = 7 Hz, OCH_2CH_3).[41]

The urethan was nitrosated with nitrogen tetroxide in ether in the presence of sodium bicarbonate. The procedure is that of White[5b], as followed by Moss.[9] *N*-Nitroso-*N*-*sec*-butylurethan was obtained as a yellow oil in 98% yield, infrared (film) 5.73 μ. The nmr spectrum showed, *inter alia*, signals corresponding to those of the urethan (cited above) at 4.45 (q, J = 7 Hz), 4.60,[42] and 1.47 (t, J = 7 Hz). The $\Delta\delta$ values (*N*-nitrosourethan–urethan) are characteristic for the *N*-nitrosourethan.[43] When stored at 0°, the *N*-nitrosourethan appeared to be stable for at least several months. Its purity was checked by nmr before each use.

Potassium Butane 2-Diazotate.—The procedure for preparing an ethereal suspension of a diazotate has been described.[9] The direct acetylation of butane 2-diazotate will be described in detail and brief remarks will be made about other procedures.

A solution of 20 mmol of Ac_2O[44] (or AcCl) in 25 ml of dry ether was rapidly injected, through a septum, into a nitrogen-blanketed suspension of 10 mmol of the diazotate at −19°. Nitrogen evolution was rapid, and complete (80–100% of theory) within 2–3 min. Butenes were removed from the evolved nitrogen (which was determined manometrically) by a sulfuric acid scrubber.

The ethereal product solution was washed with 5 ml of water, dried over $MgSO_4$, filtered, and then concentrated to about 25% of its original volume for gc analysis. The following compounds were isolated and characterized by comparison of retention times infrared spectra (and, in some cases, nmr spectra) with those of authentic samples:[45] *tert*-butyl alcohol, *sec*-butyl alcohol (acetic anhydride, acetic acid, *tert*-butyl acetate, eluted as a mixture), *sec*-butyl acetate,[46] diethyl carbonate, ethyl *tert*-butyl carbonate,[9] ethyl *sec*-butyl carbonate,[47] di-*tert*-butyl carbonate,[9] *sec*-butyl *tert*-butyl carbonate,[47] and (impure) *sec*-butylurethan.

The yield of *sec*-butyl acetate was determined by gc,[45] at 70°, of the crude product mixture, to which had been added a 2-hexanol standard. The thermal conductivity detector was calibrated for relative response, and the corrected *sec*-butyl acetate yields were 23–24% for acetylation with Ac_2O at −19°; the yield was lower in the AcCl reaction.[12]

(34) An arbitrary selection of some leading references, not necessarily those which mutually agree over interpretation, includes (a) I. N. Feit and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, **92**, 1620 (1970); (b) R. A. Bartsch, *J. Org. Chem.*, **35**, 1334 (1970); (c) R. A. Bartsch and J. F. Bunnett, *J. Amer. Chem. Soc.*, **91**, 1376 (1969); (d) **90**, 408 (1968); (e) I. N. Feit and W. H. Saunders, Jr., *Chem. Commun.*, 610 (1967); (f) H. C. Brown and R. L. Klimisch, *J. Amer. Chem. Soc.*, **88**, 1425 (1966).

(35) D. H. Froemsdorf, C. H. Collins, G. S. Hammond, and C. H. Depuy, *ibid.*, **81**, 643 (1959); A. Maccoll, *Advan. Phys. Org. Chem.*, **3**, 91 (1965).

(36) As with the stereochemistry of formation of *sec*-butyl acetate, so too with the positional and geometrical orientation of elimination to butenes, it matters not whether the butane 2-diazotate is acetylated with AcCl or Ac_2O; identical results are obtained.

(37) A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 278, gives a general procedure. Our yields were generally 80–95%.

(38) Literature bp 83° (16 Torr).[39]

(39) K. Gubbins, S. Cordin, and R. Walker, *J. Gas Chromatogr.*, **3**, 331 (1965).

(40) Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrometer.

(41) Nmr spectra were recorded on either Varian A-60 or T-60 spectrometers as *ca.* 20% solutions in CCl_4. Chemical shift values are reported as parts per million downfield from an internal TMS standard. Signal integrals were consistent with structure.

(42) Only the three low-field lines of the methine proton, $J \sim 7$ Hz, are visible; the three high-field lines fall beneath the quartet at δ 4.46. The center of the methine sextet is estimated to lie at δ 4.60.

(43) R. A. Moss, *Tetrahedron Lett.*, 711 (1966).

(44) Boiling point 139°. Purified in accord with L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. I, Wiley, New York, N. Y., 1967, p 3. The boiling point given here is 139.6°.

(45) A Varian–Aerograph A90-P3 gc was used, fitted with a 5 ft × 0.25 in., 20% SE-30 on 60/80 Gas-Chrom R column. Operating temperatures were injector, 200°; column, 78°; and detector, 200°. The He flow was 60 ml/min. The products are listed in the order of their elution.

(46) This compound was prepared from *sec*-butyl alcohol and acetyl chloride. Its infrared and nmr spectra were fully in accord with expectations.

(47) See the Results section.

When the evolved gases of the reaction were passed through a trap which had been cooled to −70°, volatile products were collected and identified by their gc retention times[48] as 1-butene, *trans*-butene, and *cis*-butene. Ether (5 ml) was distilled from the reaction vessel to the cold trap at the end of the reaction so as to ensure that the olefins had been carried over. Olefin distributions[49] appear above in the Results section and in Table III. The butene yield was determined gravimetrically. Bromination with 10% Br_2/CCl_4 of a freshly obtained butene product mixture provided 1.12 g (5.18 mmol) of a mixture of 1,2-dibromobutane and *meso*- and *dl*-2,3-dibromobutane.[50] Based upon the starting *N*-nitrosourethan, 11.5 mmol, the total butene yield was 45%.

Several variations of the fundamental decomposition procedure were employed in the optically active diazotate studies, which are summarized in Table I. The table lists all reagent quantities and reaction conditions, as well as the amounts of isolated *sec*-butyl acetate.[51] For runs which required solvents other than ether, the latter was removed *in vacuo* and the purified, dried, new solvent was injected through a septum onto the dry diazotate. All manipulations were carried out under nitrogen, and run 5 was performed in a nitrogen-filled drybox.

Optically Active Butane 2-Diazotate.—Optically active (*d*) 2-aminobutane was obtained from the racemate by the method of Bruck,[13] and was converted to the active urethan[14] as described above for the racemic series. Optical purities were determined on the *N*-*sec*-butylurethan, using Bruck's value of $\alpha^{21}D$ 18.2° as 100%. In actuality, the optically pure urethan is probably at least 2% more rotatory.[52-54]

The active urethan was nitrosated and converted to the diazotate as described above for the racemic series. Infrared and nmr spectra of the active compounds agreed with those of the previously examined racemates.

Optical rotations and analyses of *sec*-butyl acetate obtained in the acetylations of optically active butane 2-diazotate appear in Table I.[51]

In a control experiment, 0.19 g of acetic anhydride, 0.14 g of acetic acid, 0.62 g of diethyl carbonate, 0.62 g of *tert*-butyl acetate, 0.14 g of 1-butene, 1.0 g of potassium acetate, and 0.14 g of *sec*-butyl acetate ($\alpha^{25}D$ −1.25°, neat, 0.5 dm) were stirred in 10 ml of ether at 25° for 1 hr. After washing with 2.8 ml of water, we dried, filtered, and concentrated the organic material. Gc isolation at 78° from a 7 ft × 0.25 in., 20% SE-30 on 80/100 Chromosorb P column afforded 0.0592 g of the acetate which, after dilution with 0.0782 g of racemic ester, had $\alpha^{24}D$ −0.565°. The control product thus had (corrected) $\alpha^{24}D$ −1.31°.

(48) A Barber-Colman, Model 5000, flame ionization gc was employed, fitted with a 100-ft SF-96 Golay column. The detector and injector temperatures were 235° and 220°, respectively. The column was immersed in a Dry Ice–acetone bath which was held at −50°.

(49) The flame ionization detector was calibrated using prepared butene mixtures, and the relative responses, 1-butene:*trans*-butene:*cis*-butene were ~0.98:1.00:1.08. The results as given, however, are not corrected.

(50) Gc[45] at 90° showed less than 4% of impurities. Authentic dibromobutanes were obtained by brominating an authentic mixture of butenes.

(51) Full details of all gc procedures and columns used, together with a running commentary on each run, will appear in K. M. Luchter, Ph.D. Thesis, Rutgers University, New Brunswick, N. J., 1972. In general, the product was first isolated from a Carbowax 20M column, and then rechromatographed on a SE-30 column; final purity was established by reinjection and infrared analysis.

(52) Bruck, *et al.*,[14] report $\alpha^{20}D$ +5.47° and $\alpha^{19}D$ −5.56° for *sec*-butylamine and $\alpha^{21}D$ +18.2° for the *d*-urethan. Thomé[53] reports $\alpha^{20}D$ 5.38° for the amine. White has adduced evidence in support of Thomé's value.[5d] In some cases we obtained 2-aminobutane of somewhat *higher* rotation than yet reported (*e.g.*, $\alpha^{27}D$ +5.94°). Yet after conversion to the urethan, rotations lower than 18.2° were obtained. We have no explanation for this behavior. The amine in question was distilled from sodium, and was gc pure. All optical purities above *could*, therefore, be too low by 2–8% of the listed values. This would have no effect on our discussion or conclusions.

(53) L. G. Thomé, *Chem. Ber.*, **36**, 582 (1903).

(54) Optical rotations were measured with a Rudolph polarimeter, using a 100-μl, 0.5-dm cell. Samples were diluted with racemic material when necessary. In several cases, readings were checked, with good agreement, on a Perkin-Elmer spectropolarimeter.

***N*-Nitroso-*N*-*sec*-butylacetamide.**—*N*-*sec*-Butylacetamide was made from 2-aminobutane by the general procedure of White,[5c] and had bp 60–63° (0.15–0.25 Torr) and a C=O absorption (neat) centered at ~6.1 μ in the infrared.[55] The preparation of optically active *N*-*sec*-butylacetamide from the active amine was similarly accomplished. Our sample had $[\alpha]^{24}D$ +15.89° ($CHCl_3$, *c* 6.063 × 10^{-2}) and was 95.8% optically pure.[5d]

The nitrosation of the amide was modeled after the procedure of White.[5b] A three-neck flask was fitted with an inlet tube, low-temperature thermometer, stirring bar, and rubber septum. The flask was charged with 15 ml of ether and 30 mmol of sodium acetate. After cooling the flask (Dry Ice–acetone bath, −60°), nitrogen tetroxide (20–30 mmol) was admitted through the inlet tube. The reaction mixture was warmed to −5°, 10 mmol of *N*-*sec*-butylacetamide in 5 ml of ether was injected through the septum, and then the nitrosation was allowed to proceed, with stirring, for 1 hr at −10 to 0°. Light was excluded.

Work-up was done in the cold room (<15°). The ethereal product mixture was washed twice with saturated sodium bicarbonate solution, then with water, and then dried over molecular sieves. A 10-ml ethereal back-extract of the aqueous washes was combined with the major ether phase.

The dried ethereal *N*-nitroso-*N*-*sec*-butylacetamide[56] was decanted into a three-neck flask containing a stirring bar, a gas outlet tube, and a thermometer. The flask was connected either to a sulfuric acid scrubber, and thence to a gas buret, or to a cold trap (butene isolation). The contents of the flask were stirred in the dark at 28–30° for 15–18 hr, at which time gas evolution was over. The ether solution was washed with saturated aqueous sodium bicarbonate, then with water, and then dried. After filtration and concentration of the reaction product, *sec*-butyl acetate was isolated by gc (see above). The yield of the acetate, determined as before against a 2-hexanol standard, was 13.3–17.9% over two experiments.

The butene products were collected at −70°, in a separate run. The ether reaction solvent was distilled into the trap to ensure that all of the butenes had been purged from the reaction vessel. The 1-butene:*trans*-butene:*cis*-butene distribution was 3.85:2.38:1 as determined at 40° on the 20% SE-30 column described above.

In Table II, there will be found the conditions employed in the several decompositions of the optically active *N*-nitroso-*N*-*sec*-butylacetamide, as well as the optical rotations of the product *sec*-butyl acetate. The pure ester was isolated by iterative gc on the SE-30 column.

There were several unexplained infrared absorptions in the product of run 1 (Table II) at 4.55, 5.55, and 13.2 μ. The high optical rotation for this run's product may therefore be spurious. The *sec*-butyl acetate from runs 2 and 3 still contained an absorption at 13.2 μ which is absent in the racemic product. However, rechromatography of these samples on both SE-30 and Carbowax 20M columns revealed no impurities.

Registry No.—Butane 2-diazotate, 21892-73-9; *sec*-butyl acetate, 105-46-4; *N*-nitroso-*N*-*sec*-butylbenzamide, 33189-79-6; *N*-nitroso-*N*-*sec*-butylurethan, 33124-25-3.

Acknowledgments.—We thank the National Science Foundation (GP-12645) and the National Institutes of Health (GM-13585) for financial support. R. A. M. thanks the National Institutes of Health for a Special Postdoctoral Fellowship, and the Department of Chemistry, Massachusetts Institute of Technology, for its hospitality during the composition of the manuscript.

(55) Literature bp 119° (18 Torr), C=O at 6.06 μ (CCl_4 solution).[5b]

(56) A sample isolated by distillation of the ether at 0° had a C=O absorption in the infrared at 5.8 μ (neat); this is the expected location.[5b]