The Direct Introduction of the Diazo Function in Organic Synthesis[1]

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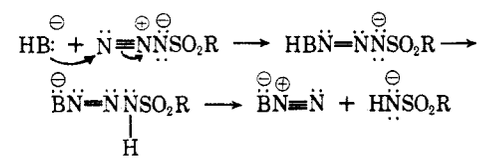
Received March 1, 1968

For synthetic purposes, introduction of the diazo function at methylene positions flanked by two carbonyl groups proceeds smoothly with tosyl azide–sodium hydride or *p*-carboxybenzenesulfonyl azide–triethylamine and leads to no separation problems after reaction. With methine positions the same introduction of diazo occurs with cleavage of one acyl residue as with an N-sulfonylamide. Hydrolysis of diazo diketones with alkali is extremely facile so that several variations on these reactions allow the synthesis of most diazo ketones and esters. Methylene or methine positions flanked by phenyl and carbonyl also react, resulting chiefly in diazo compounds or Wolff rearrangement products, depending on experimental conditions. This method represents a substantial broadening of utility for the Wolff rearrangement as a synthetic tool. The diazo transfer reaction also converts primary amines (as their Grignard salts) into azides, and reactions with nitroalkanes, phenols, indoles, and Grignard reagents are also described briefly.

The diazo function is potentially a more valuable synthetic tool than is presently recognized because of its high reactivity, but its utility has heretofore been limited by a scarcity of good methods for producing it.[2] Therefore, a number of years ago we undertook to examine new synthetic procedures for introduction of the diazo function, particularly by the *diazo transfer reaction*.[3,4] About the same time this reaction came under concentrated study by Regitz and his group, and he has recently reviewed their results and those of others.[4] Our central criterion in this work was one of synthetic value, dictating not only acceptable yields but also mild conditions and easy separation of the often rather unstable diazo compounds from other products. Thus, while much of our work corroborates the results of Regitz's group, our approach has led to some useful synthetic variations and explored some different substrates.

Diazo transfer involves anionic attack on a reagent consisting of N_2^+- attached to a leaving group; the usual reagent is a sulfonyl azide and the general course of the reaction, summarized in eq 1, was first analyzed and successfully utilized by Doering and DePuy.[5]



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The reaction of various 1,3-dicarbonyl active methylene compounds was examined first since a number of their 2-diazo derivatives were known compounds and relatively stable. Reaction of such active methylene compounds with toluenesulfonyl (tosyl) azide and triethylamine in methylene chloride did in fact produce the diazo derivatives in fair yield in about half an hour, but isolations were rendered difficult by the problems of separating the diazo products from toluenesulfonamide and unreacted tosyl azide. Several variations in conditions were then examined with a view to simplifying product isolation.

When sodium hydride was used as the base in tetrahydrofuran, the sodium salt of toluenesulfonamide precipitated cleanly from the solution, allowing a facile separation from the desired diazo compound. In many circumstances this was found to be a clean procedure. Variation of the reagent so as to provide water-soluble by-products was also examined, first in the form of N,N-dimethylsulfamoyl azide [$(CH_3)_2NSO_2N_3$], the product sulfamide of which is cleanly extracted by mild aqueous acid; this reagent gave a 61% yield of pure diazodimedone when allowed to react with dimedone in ether–triethylamine. However, it appeared to be desirable in some cases to have an excess of azide reagent and neither of these two procedures can be so used without encountering difficulty in separating the excess azide from diazo product.[6]

Accordingly, we synthesized *p*-carboxybenzenesulfonyl azide to provide a solubility handle on the reagent molecule. The lithium and triethylamine salts of this acid are soluble in tetrahydrofuran and acetonitrile, respectively. The triethylamine salt of its product *p*-carboxybenzenesulfonamide is essentially insoluble in acetonitrile. In a standard procedure the carboxy azide is suspended in acetonitrile and dissolved by addition of excess triethylamine.[7] Addition of the active methylene substrate results in precipitation of the carboxyamide salt usually within an hour. Filtration, addition of methylene chloride, and washing with aqueous base then affords diazo compound in a relatively uncontaminated state, the yield of diazodimedone being 86%. Examples are summarized in Table I. This procedure we found to be the most satisfactory of the several examined for 1,3-dicarbonyl compounds.[8]

Methylene groups activated by only one carbonyl function were unreactive,[9] cyclohexanone and acetophenone being recovered largely unchanged either

(1) A preliminary joint communication with Professor Yates' group containing some of the present material has appeared: M. Rosenberger, P. Yates, J. B. Hendrickson, and W. A. Wolf, *Tetrahedron Lett.*, 2285 (1964).

(2) *Cf.* the review by H. Zollinger, "Diazo and Azo Chemistry," Interscience Publishers, Inc., New York, N. Y., 1961.

(3) The reaction described here, a transfer of an intact diazo moiety to an anionic site, is labeled a *diazo transfer reaction* to distinguish it from diazotization, a process in which the N–N bond is created in the reaction.[4]

(4) M. Regitz, *Angew. Chem. Intern. Ed. Engl.*, **6**, 733 (1967).

(5) W. Doering and C. DePuy, *J. Amer. Chem. Soc.*, **75**, 5955 (1953).

(6) Dimethylsulfamoyl azide can be removed with repeated aqueous acid extraction, but such extended exposure to acid can lead to some decomposition of the diazo product in sensitive cases.

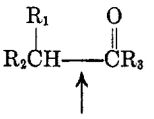
(7) As a test of the stability of the reagent under these conditions, the triethylamine reagent solution was left at room temperature for 2 days and the azide was recovered in 95% yield.

(8) Use of hydroxide or methoxide as bases[4] produce serious practical complications owing to their ready attack at sulfonyl, displacing azide ion. Several experiments using *t*-butoxide as base appeared to offer no advantage. In one attempt at acid catalysis, desoxybenzoin, tosyl azide, and toluenesulfonic acid produced no reaction overnight. While this may not be conclusive, we never seriously pursued the exploration of acid-catalyzed diazo transfer since the product diazo compounds are known to be very sensitive to acid.

(9) Under various different basic media employed by Regitz[4] the same results were observed.

TABLE I

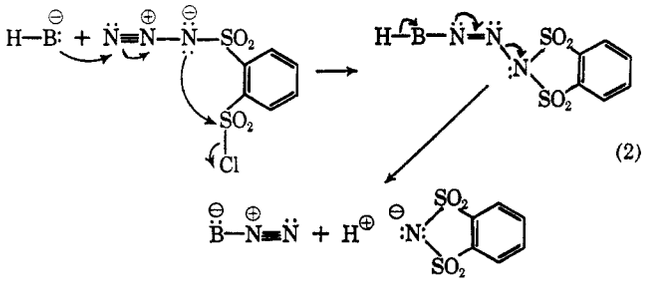
DIAZO TRANSFER TO CARBONYL COMPOUNDS



Compound	R_1	R_2	R_3	Method[a]	Results[b]	Yield, %
Acetylacetone	H	$COCH_3$	CH_3	B	1	83
Dimedone	H	$COCH_2C(CH_3)_2$——CH_2		B	1	86
Ethyl acetoacetate	H	$COOC_2H_5$	CH_3	B	1	84
Diethyl malonate	H	$COOC_2H_5$	OC_2H_5	B	1	76
Oxindole	H	*o*-C_6H_4——NH		B	1	67
Cyclohexanone (hydroxymethylene-)	$CH_2CH_2CH_2CH_2CO$		H	D	2	52[c]
Ethyl α-methylacetoacetate[d]	CH_3	$COOC_2H_5$	CH_3	A	2	63
Benzylacetylacetone	$CH_2C_6H_5$	$COCH_3$	CH_3	B	2	82
Desoxybenzoin	H	C_6H_5	C_6H_5	A	1	56
					3	2
				B	3	75
				C	3	44
Phenylacetone	H	C_6H_5	CH_3	A	1	61
					3	4
				C[d]	3	30
Dibenzyl ketone	H	C_6H_5	$CH_2C_6H_5$	A	3	46
				C	3	~45
Phenylacetaldehyde	H	C_6H_5	H	C	3	46
1,1-Diphenylacetone[d]	C_6H_5	C_6H_5	CH_3	A	2	23
					4	~15
Diphenylacetaldehyde[d]	C_6H_5	C_6H_5	H	A	2	⩾30
					3	46
					4	~15
2-Phenylpropionaldehyde	CH_3	C_6H_5	H	A	2	~20
					3	24
					4	31
				B[d]	3	28

[a] A = T_sN_3–NaH–THF; B = *p*-$HOOCPhN_3$–Et_3N–CH_3CN; C = T_sN_3–Et_3N–CH_3CN; D = $Li^{\oplus\ominus}OOCPhN_3$–THF + enolate salt–$Et_2O$. [b] Compare Chart II. 1, simple diazo transfer (R_1 = H); 2, diazo transfer with acyl cleavage at arrow; 3, Wolff rearrangement (R_3 migration across bond marked with arrow); 4, ketone formation; cleavage at arrow. [c] Over-all yield: formylation followed by diazo transfer directly. [d] Reaction incomplete by methods B or C.

with the standard procedure above or with tosyl azide–sodium hydride. Methylene flanked by ketone and phenyl is reactive,[9] although discussion of the more complex results here is deferred to a later paragraph. We considered one approach, however, to making the reagent more reactive to compensate for less reactive anionic sites. We argued that, if the initial sulfonyl triazine anion produced by attack of the carbonion on sulfonyl azide (eq 1) could internally displace a good leaving group provided in the reagent molecule, the equilibrium should be sharply shifted to the right. Accordingly, we proposed the synthesis of *o*-chlorosulfonylbenzenesulfonyl azide and the reactions outlined in eq 2. The second step should also be



(2)

enhanced by the excellent stabilization available to the disulfonimide anion which acts as the second leaving group; *o*-benzenedisulfonimide is fully ionized in (and not extractable from) water and said to be as strong an acid as HCl.[10] At present it is not clear which of the two steps in eq 1 or 2 is rate determining.

Reaction of sodium azide and *o*-benzenedisulfonic anhydride yielded the monoazide monosulfonate salt, but attempts to convert the sulfonate into sulfonyl chloride with chlorosulfonic acid or thionyl chloride led only to starting material whereas phosphorus pentachloride yielded material with no azide group remaining in the ir spectrum. However, reaction of equimolar amounts of tetrabutyl ammonium azide with *o*-benzenedisulfonyl chloride[10] in methylene chloride yielded a crystalline product which was substantially the desired compound, contaminated with only a small amount of the dichloride. When this azide–chloride was tested with acetoacetic ester under either triethylamine or sodium hydride catalysis, only a small yield of the diazo derivative and substantial unreacted reagent were recovered under conditions in which the transfer reaction was substantially complete with tosyl azide. The *ortho* substituent therefore appears to offer no assistance in rate over tosyl azide; as other internal-assistance possibilities are still being examined, no speculation as to the failure of this model is offered at present. Two further reagents, *p*-nitrobenzenesulfonyl azide and picryl azide, were also compared against the tosyl azide reagent but both gave substantially poorer results.

(10) W. R. H. Hurtley and S. Smiles, *J. Chem. Soc.*, 129 (1824).

Having explored several reagents and various conditions to optimize diazo transfer in the model cases of β-dicarbonyl compounds with methylene anion sites, we turned to the case of β-dicarbonyl compounds with only one α hydrogen.[1,4] Reaction with simple azides still occurs, proceeding to a diazo compound by cleavage of the original β-dicarbonyl moiety as in eq 3. The

$$\underset{\underset{R'}{|}}{RCOCHCOR''} + C_6H_5SO_2N_3 \xrightarrow{\text{base}} \underset{\underset{R'}{|}}{RCOCN_2} + R''CONHSO_2C_6H_5 \quad (3)$$

reaction is still a facile one, proceeds in good yield, and affords diazo ketones or diazo esters depending on the starting material. The by-product N-sulfonylamides are acidic enough to allow their easy removal by extraction with aqueous base. Of the two original carbonyl functions, the order of preference for cleavage appears to be -CHO > -COR > -COOR from the cases examined, which are shown in Table I. We presume that the cleavage of the acyl moiety proceeds by internal attack of the sulfonamide anion before its release into solution, as discussed further below.

The ready cleavage of 1,3-dicarbonyl compounds under these conditions suggested that hydrolysis of their 2-diazo derivatives should also occur, and this was found to be the case. When 3-diazo-2,4-pentanedione was dissolved in acetonitrile and sodium hydroxide added, diazoacetone could be isolated in a pure state in 90% yield after 1 hr. In other cases, the diazo transfer reaction in acetonitrile was simply followed by addition of hydroxide and subsequent working up after allowing adequate contact time for hydrolysis. This procedure produced ethyl diazoacetate in 69% over-all yield from ethyl acetoacetate in about 2 hr; this is easily the simplest present preparation of ethyl diazoacetate.

The hydrolytic cleavage of diazo ketones is summarized in eq 4. When R = R''CO- or R''OCO- as

$$\underset{\underset{N_2}{\|}}{\overset{}{RC}}\!\!-\!\!\underset{\underset{O}{\|}}{CR'} \xrightarrow{-OH} \underset{\underset{N_2}{\|}}{RCH} + R'COOH \quad (4)$$

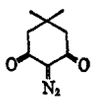
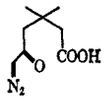
in the above cases, the cleavage presumably owes its facility to stabilization of the product diazo carbanion by an adjacent carbonyl. With phenyl as stabilization (R = aryl), as in diazodesoxybenzoin,[11] the cleavage requires more vigorous conditions while simple aliphatic diazo ketones (R = alkyl) are unaffected. Furthermore, under the room temperature conditions used here, esters adjacent to the diazo function (R' = OR'') are unaffected (*cf.* diazomalonate is unreactive), the order of preference apparently being R' = H > alkyl > aryl > OR''. The results are summarized in Table II.

From a synthetic vantage point the last two variants allow in principle the production of virtually any diazo ketone or diazo ester from the parent carbonyl compound. Firstly, the α-methylene site may be formylated, and the resultant anion of the hydroxymethylene derivative may be used directly for the diazo transfer reaction. In such an example we formylated cyclohexanone and treated the product

(11) P. Yates and B. Shapiro, *J. Org. Chem.*, **23**, 759 (1958).

TABLE II

HYDROLYSIS OF DIAZO KETONES

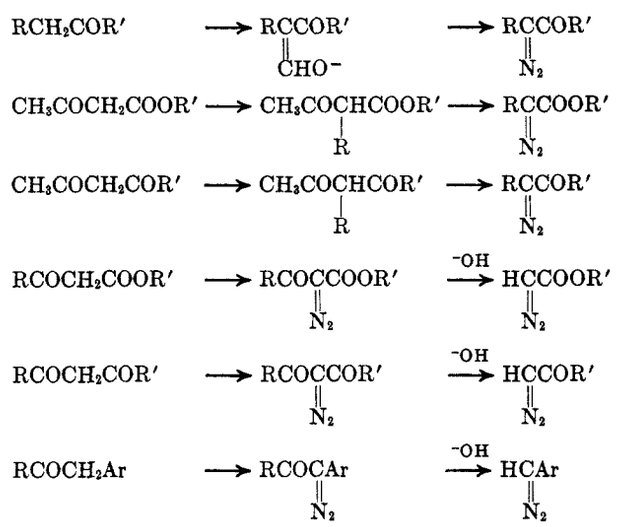
Diazo ketone	Reaction[a] time	Product[a]	Yield, %
$C_6H_5COCN_2C_6H_5$	Overnight	$C_6H_5CHN_2$	70[b]
$C_6H_5COCN_2COC_6H_5$	Overnight	$C_6H_5COCHN_2$	85
$CH_3COCN_2COOC_2H_5$	5 min	$HCN_2COOC_2H_5$	69[c]
$CH_3COCN_2COCH_3$	60 min	CH_3COCHN_2	90
	Overnight		86[d]

[a] Reaction with 1 *N* alkali in aqueous acetonitrile at room temperature. The products listed were unchanged on further standing in this medium as were diethyl diazomalonate, ethyl α-diazopropionate, and $C_6H_5CH_2CN_2COCH_3$. [b] Concentrated aqueous alkali in methanol–ether at room temperature. [c] Over-all yield from diazo transfer followed by hydrolysis as above for the indicated time. [d] Crude yield of unstable acid product; see Experimental Section.

carbanion directly in the same vessel with the lithium salt of *p*-carboxybenzenesulfonyl azide to produce diazocyclohexanone in 52% yield. Secondly, the acetoacetic ester or related acetylacetone syntheses may be used, monoalkylation being followed by diazo transfer with concomitant cleavage of acetyl. Finally, a 2-diazo-1,3-dicarbonyl compound may be prepared, and one of the acyl groups may be subsequently cleaved by mild alkaline hydrolysis. These synthetic variants are summarized in Chart I.

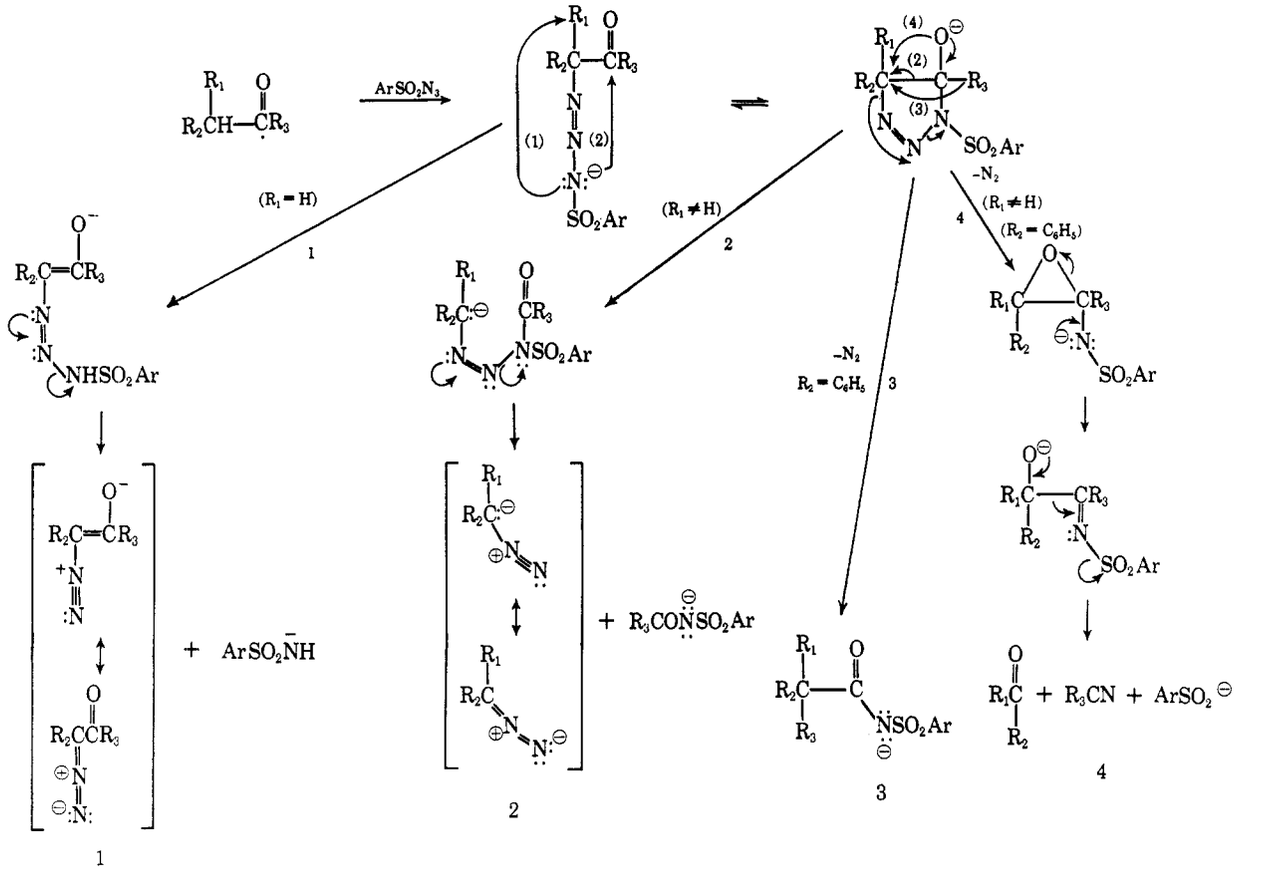
CHART I

FORMATION OF DIAZO COMPOUNDS. SYNTHETIC VARIATIONS



While the diazo transfer reaction thus appears to be of rather broad utility as described above for cases in which the reaction site is activated by two adjacent carbonyl functions, we encountered some interesting surprises in the less activated cases in which the reactive methylene or methine is flanked by carbonyl and phenyl. The first unexpected result was the observation that, whereas the sodium hydride–tosyl azide method gave a 56% yield of the expected diazo ketone from desoxybenzoin, the triethylamine–*p*-carboxybenzenesulfonyl azide method produced no diazo ketone but only the Wolff rearrangment product, N-(*p*-carboxybenzenesulfonyl)diphenylacetamide, in 75% yield. The same dichotomy was exhibited with phenylacetone, and, in the other cases with methylene

CHART II
COURSE OF DIAZO TRANSFER

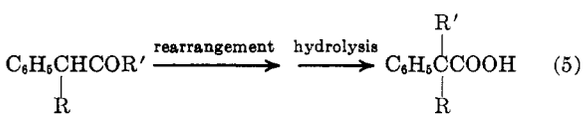


sites, phenylacetaldehyde and dibenzyl ketone, only Wolff rearrangement resulted with either method.[12]

However, when only a single α hydrogen was available next to the carbonyl (methine sites), with the expectation that reaction could only proceed with acyl cleavage, a new pathway intervened. Thus both 1,1-diphenyl acetone and diphenylacetaldehyde produced some diphenyldiazomethane by acyl cleavage as anticipated but also a significant yield of benzophenone, and in the latter case a substantial yield of the Wolff rearrangement product as well. In all the methine cases, only the sodium hydride method afforded complete reaction, the weaker base triethylamine leaving substantial starting material in each trial. These results are summarized in Table I.

A summary of the four pathways observed in these diazo transfer reactions is provided in Chart II with presumptive mechanisms supplied. Route 1 is available only with methylene reaction sites (R_1 = H) and leads to simple diazo transfer with loss of sulfonamide. This is the only course of reaction when a methylene site is flanked by two carbonyls and substantially the only course with $C_6H_5CH_2CO$– compounds when sodium hydride is used as the base. Route 2 occurs only with methine sites ($R_1 \neq$ H) and leads to diazo transfer with concomitant acyl cleavage. With β-dicarbonyl compounds this is a clean, high-yield reaction with either base, while with C_6H_5CH–CO– compounds this route is but one of several. Route 3, the Wolff rearrangement, occurs only in the phenyl compounds (R_2 = C_6H_5). It is the major pathway in reactions catalyzed by triethylamine although with methine sites such catalysis is apparently inadequate, leading to incomplete reaction. With sodium hydride this route is very minor except in cases bearing a very effective migrating group ($C_6H_5CH_2$– or H–).[13] The production of a ketone at the anionic site, rationalized mechanistically in route 4, was an unexpected result, and in no case studied did it constitute a major reaction pathway. Like the Wolff rearrangement, this route was observed only in the phenyl cases (R_2 = C_6H_5); unlike that rearrangement, it was observed only in methine cases (R_1 = H). The postulated mechanism draws on ample precedent in base-catalyzed epoxide formation, the abnormal Beckmann reaction, and the known occurrence of sulfinate anion leaving group in a number of base-initiated reactions.

The synthetic value of the Wolff rearrangement has hitherto been limited to the Arndt–Eistert homologation process for a diazomethyl ketone and photochemically initiated rearrangement of some other diazo ketones.[2] The present observations suggest that this carbon skeleton rearrangement (or ring contraction) may now be usefully extended to a number of other ketones, most clearly α-aryl ketones, as summarized in eq 5 for synthesis purposes.

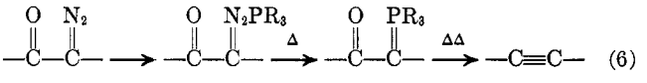


(5)

(12) Using different bases, Regitz[4] also observed both products but apparently not with the clean predominance of either.

(13) In aldehyde cases (R_2 = H) the same result is produced by this route whether the hydrogen migrates (internal transfer) or is removed by base to form the enolate of the N-sulfonylamide product with loss of nitrogen. We made no effort to distinguish these possibilities in this study.

The major reaction of diazo compounds in acid is protonation on carbon followed by loss of nitrogen and appropriate collapse of the resultant carbonium ion. Their reactions with bases are less common and less well understood but most often appear to involve addition of the base to nitrogen.[2] Such addition products are the phosphorazines formed by addition of triphenylphosphine to diazo ketones, eq 6; these



(6)

derivatives are more stable than the parent diazo ketones (higher melting and more highly crystalline) and have often been used to characterize diazo ketones. We were interested to see whether they show similar reactivity. Using diazoacetophenone as a test it was found, however, that, while the diazo ketone itself cleanly afforded ω-acetoxyacetophenone on warming (65°) in acetic acid, the phosphorazine was unreactive under these conditions. Addition of catalytic boron trifluoride etherate caused some decomposition but yielded none of the acetoxy derivative; similar negative results attended the attempts to decompose the triphenylphosphine adduct of diazodesoxybenzoin. As to other phosphorazines, diazoacetophenone was unreactive to triphenylphosphite, gave only an oily derivative with tributylphosphine, and afforded ω-chloroacetophenone in 58% yield with phosphorus trichloride. On the other hand, gentle warming of phosphorazines causes elimination of nitrogen and formation of phosphonium ylides, so that diazo compounds produced by diazo transfer can be converted into these Wittig reagents, and further pyrolysis of the α-keto ylides (ketophosphoranes) produces acetylenes in a number of cases[14] (eq 6).

Other Anionic Substrates.—Turning our attention to other anionic sites, we briefly investigated diazo transfer to acceptors other than enolate. Under our various conditions, phenol afforded only phenyl tosylate with no sign of diazo transfer to carbon to yield a diazo oxide, although Regitz[4] observed this in low yields on β-naphthoxide and also obtained the azo dimer. Nitromethane and nitrocyclohexane were found to be unreactive to the standard methods while ethyl nitroacetate was excessively exothermic even with triethylamine catalysis although pyridine catalysis gave the diazo derivative in 8% yield.[15] 3-Nitro-2-butanone gave a crude product which appeared to contain a small amount of diazo compound but was not pursued further.

The reaction of indole, as its Grignard salts, with tosyl azide was violent at room temperature, leading only to dark tars, whereas, if the mixture is made at −70° and allowed to warm slowly, reaction sets in suddenly at an intermediate temperature with the same result. Past attempts to prepare 3-diazoindolenine have also led to tars, presumably by polymerization of the product once formed.[16] In our case, the expected tosylamide product was in fact isolated. Accordingly, we attempted the reaction on indoles blocked at the 2 position; oxindole was converted into its diazo derivative very easily (Table I). 2-Methylindole in the sodium hydride procedure produced the dimeric 3-azo-2-methylindole, presumably by diazo transfer yielding the desired 3-diazoindolenine followed by attack of a second indole 3 anion on the diazo nitrogen, whereas 2-phenylindole rapidly afforded the desired 2-phenyl-3-diazoindole in 83% yield. 2-Carbethoxy-5-methoxyindole did not react overnight in the sodium hydride method.

Grignard reagents attack tosyl azide vigorously; at −70° a 7% yield of diazomethane was produced from methylmagnesium iodide. Phenylmagnesium bromide at −70° afforded phenyl diazonium salts as shown by the isolation of phenol (35%) after hydrolysis, but the major product was biphenyl (53%). Whether this represents a practical synthesis of symmetrically substituted biphenyls was not investigated further.

Finally, we considered that primary amines (or their anions) should react in the diazo transfer reaction to form azides. Such a conversion should be very useful in synthesis as a nonbasic protecting group for amines which would be cleanly removable at will by reduction[17] but relatively impervious to acid or base. Accordingly, we attempted the diazo transfer reaction on aniline and *n*-butylamine with triethylamine and with sodium hydride catalysis (and with no catalysis) and recovered only starting amines in each case. However, when methylmagnesium iodide was added to the amine first to form the Grignard salt, RNHMgI, reaction with tosyl azide proceeded to produce the azide in less than an hour at room temperature, affording the following yields from the amines: aniline, 47%; cyclohexylamine, 47%; *n*-butylamine, 24%; benzylamine, 23%.[18] Presumably the yields will be increased by reason of a cleaner work-up procedure if the *p*-carboxy reagent is utilized instead, but this has not yet been investigated. By analogy with the acyl cleavage route above, we expected that the salts of amides, RNNCOR′, should also be converted into azides and N-acylsulfonamides, but a variety of attempts with Grignard and other bases afforded only unchanged amides. Further work is in progress to develop this reaction as a synthetically useful tool and to explore the reaction with secondary amine salts as well.

Experimental Section[19]

***p*-Carboxybenzenesulfonazide.**—To 25 g (0.104 mmol) of *p*-carboxybenzenesulfonic acid monopotassium salt (Aldrich) was slowly added 34 ml of freshly distilled chlorosulfonic acid; the mixture was heated at 100° for 2 hr. The solution was cooled and dripped onto ice as quickly as possible and filtered, and the precipitate was dried to give 21.1 g (85%) of *p*-carboxybenzenesulfonyl chloride, mp 235–237° (lit.[20] mp 235°). The chloride was dissolved in 300 ml of warm acetone, and 7.80 g (0.12 mol) of sodium azide in 50 ml water was added. More water was added until the reaction became one phase. After 1.5 hr, the solution was poured into 2.5 l. of water and filtered. Recrystallization of the white solid from ether gave, in three crops, 15.62 g (72%) of *p*-carboxybenzenesulfonazide: mp 184–186°; ir, 4.63, 5.88, 7.76, 8.5 μ.

(14) S. Trippett and D. Walker, *J. Chem. Soc.*, 3874 (1959).

(15) H. Balli and V. Müller, *Angew. Chem. Intern. Ed. Engl.*, **3**, 644 (1964); H. Balli and R. Low, *Tetrahedron Lett.*, 5821 (1966).

(16) R. Moore and P. Wortach, Jr., British Patent 816,382 (to General Aniline and Film Corp.); *Chem. Abstr.*, **55**, 188 (1959).

(17) P. A. S. Smith, "The Chemistry of Open-chain Organic Nitrogen Compounds," Vol. 2, W. A. Benjamin Co., New York, N. Y., 1966, p 251.

(18) The same reaction was independently discovered about the same time by W. Fischer and J. P. Anselme, *J. Amer. Chem. Soc.*, **89**, 5284 (1967).

(19) Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were taken in methylene chloride on a Perkin-Elmer Infracord. Nmr spectra were preformed on a Varian A-60a using tetramethylsilane as internal standard.

(20) S. Smiles and D. Harrison, *J. Chem. Soc.*, 2022 (1922).

Anal. Calcd for $C_7H_5N_3O_4S$: C, 37.00; H, 2.20; N, 18.50; S, 14.10. Found: C, 36.77; H, 2.24; N, 18.57; S, 14.29.

Reaction of Azides with Hydroxide and Benzoate Anions. A.—Tosyl azide (158 mg) was dissolved in 10 ml of saturated KOH–methanol and stirred overnight. Filtration and evaporation gave a white powder whose ir spectrum was almost identical with that of sodium tosylate. Treatment of this with PCl_5 at 150° for 4 hr followed by heating with aqueous ammonium hydroxide gave tosylamide: mp 134–136°, mmp 134–136° with an authentic sample.

B.—To a solution of 494 mg (1.36 mmol) of dry tetrabutylammonium benzoate (prepared by mixing equimolar amounts of tetrabutylammonium hydroxide and benzoic acid) in methylene chloride was added 197 mg (1 mmol) of tosyl azide. After 1 day, little change was noted in the ir spectra. After 5 days, the spectra had definitely changed. The solution was extracted with water and chromatographed on silica to give 68 mg (46%) of benzoyl azide (identical in all respects with an authentic sample), 30 mg (15%) of tosyl azide, and several milligrams of an oil whose spectrum was consistent with tosyl benzoate.

C.—To a solution of 158 mg (0.80 mmol) of tosyl azide in 80% ethanol was added 2 mmol of sodium benzoate. After 3 days, work-up gave back only tosyl azide (150 mg).

D.—*p*-Carboxybenzenesulfonazide (100 mg) was suspended in acetonitrile and excess triethylamine added, upon which the azide went into solution. Work-up after 2 days gave 96 mg of starting azide.

Diazodimedone (2-Diazo-5,5-dimethylcyclohexa-1,3-dione).—*p*-Carboxybenzenesulfonazide (120 mg, 0.50 mmol) was suspended in a stirred solution of 70 mg (0.50 mmol) of dimedone in 2 ml of acetonitrile. The mixture was cooled in an ice bath, and 152 mg (1.52 mmol) of triethylamine was added all at once, upon which the azide went into solution. The ice bath was removed, and the reaction was stirred for 15 min, filtered, poured into ether, and extracted with water. The aqueous layer was extracted with methylene chloride, and the two organic layers were combined, washed with 1 *M* sodium hydroxide and water, dried, and evaporated to give 76 mg (96%) product, mp 100–103°. Recrystallization from ethanol–petroleum ether (bp 30–60°) gave 72 mg (86%): mp 107–109° (lit.[21] mp 106–108°); ir, 4.65, 6.07 μ.

Other Active Methylene Compounds.—The following diazo compounds were prepared by the same procedure, differing only in contact time as shown (esters were slower to react).

A.—Ethyl acetoacetate (72 mg) reacted in 90 min to yield ethyl diazoacetoacetate (73 mg, 84%) as an oil with ir (4.67, 5.83, 6.14 μ) and nmr spectra identical with those of authentic distilled material; its triphenylphosphine adduct had mp 90° (lit.[22] mp 90°). In this experiment the filtered solid was dissolved in water and acidified with concentrated HCl, and the precipitate was filtered and dried to yield 75 mg (67%) of *p*-carboxybenzenesulfonamide: mp 282–285°, mmp 280–285° with an authentic sample (prepared by heating the sulfonyl chloride with aqueous ammonia).

B.—2,4-Pentanedione (50 mg) reacted in 15 min to yield 3-diazo-2,4-pentanedione (52 mg, 83%) as an oil with ir (4.70, 6.00 μ) and nmr [τ 7.50 (s)] spectra in accord. The product was further identified by hydrolysis to diazoacetone (below), and by formation of its triphenylphosphine adduct, mp 98° (lit.[23] mp 97–98°).

C.—Diethyl malonate (80 mg) was allowed to react overnight to yield diethyl diazomalonate (71 mg, 76%) as an oil: ir, 4.69, 5.71, 5.80 μ; identified further as its adduct with triphenylphosphine, mp 88° (lit.[22] mp 92°).

D.—Oxindole (67 mg) was allowed to react overnight to yield 3-diazooxindole (55 mg, 67%): mp 158–160° (lit.[24] mp 161°); ir 2.89, 4.77, 5.90 μ.

Diazocyclohexanone.—A solution of 49 mg (0.5 mmol) of cyclohexanone and 55 mg (0.75 mmol) of dry ethyl formate in 1 ml of ether was slowly added to a stirred suspension of 50 mg (2 mmol) of NaH washed free of oil in 2 ml of ether. The reaction was stirred overnight and cooled in an ice bath, and 245 mg (1 mmol) of the lithium salt of *p*-carboxybenzenesulfonazide in 1 ml of tetrahydrofuran added slowly. After 4 hr the reaction was filtered, extracted once with water, and five times with 1 *N* NaOH. Evaporation of solvent gave 33 mg (52%) product, identical in every respect with authentic material prepared by the method of Yates and Rosenberger.[1]

Ethyl α-Diazopropionate.—A solution of 550 mg (3.82 mmol) of ethyl α-methylacetoacetate in 2 ml of dry THF was slowly added to a stirred suspension of 300 mg (7.5 mmol) of 60% NaH–oil in 5 ml of tetrahydrofuran. The reaction was cooled in a water bath and 6 mmol of tosyl azide were added slowly. After 30 min the orange reaction was filtered, poured into pentane, filtered again, extracted with water, concentrated on the rotary evaporator, and distilled at room temperature and high vacuum into a Dry Ice cooled trap, yielding 316 mg of product (63%) as a yellow oil: ir, 4.81, 5.94 μ; nmr ($CDCl_3$), τ 8.05 (s, 3 H), 5.63 (q, J = 7 cps, 2 H), 8.73 (t, J = 7 cps, 3 H).

The solid precipitated by the addition of pentane was dissolved in water, acidified with concentrated HCl, and extracted with methylene chloride. Evaporation of solvent and recrystallization from water gave, on drying, 641 mg (79%) of N-tosylacetamide, mp 133–135° (lit.[25] mp 137°). The product was further characterized as the triphenylphosphine adduct. Diazo ester (282 mg, 2.2 mmol) was added to 524 mg (2.0 mmol) of triphenylphosphine in 5 ml of ether. After standing overnight, several drops of petroleum ether were added, and the mixture was cooled giving, in two crops, 418 mg (54%) of yellow needles: mp 127–128.5° dec; ir, 5.93, 7.62, 9.0–9.4 μ; nmr ($CDCl_3$), τ 2.0–2.8 (m, 15 H), 5.80 (q, J = 7 cps, 2 H), 7.76 (s, 3 H), 8.77 (t, J = 7 cps, 3 H).

If the reaction is done in acetonitrile using *p*-carboxybenzenesulfonazide and triethylamine, it is only partially complete after a week. Mixing the products (ethyl α-diazopropionate and N-acetyl-*p*-carboxybenzenesulfonamide) in acetonitrile in the presence of triethylamine does not give rise to any starting material, showing that there is no equilibrium.

4-Phenyl-3-diazo-2-butanone.—*p*-Carboxybenzenesulfonazide (130 mg, 0.55 mmol) was suspended in a stirred solution of 94 mg (0.5 mmol) of 3-benzyl-2,4-pentanedione[26] in 2 ml of acetonitrile. The mixture was cooled in an ice bath and 2 mmol of triethylamine added, upon which the azide went into solution. After 18 hr the reaction was poured into methylene chloride and extracted three times with 1 *N* sodium hydroxide. Evaporation of the organic layer gave 72 mg (82%) of product as a light yellow oil: ir, 4.83, 6.11 μ; nmr ($CDCl_3$), τ 2.70 (s, 5 H), 6.33 (s, 2 H), 7.75 (s, 3 H).

The product was further characterized as the triphenylphosphine adduct. Excess triphenylphosphine was added to an ether solution of 70 mg (0.40 mmol) of the diazo ketone. After standing overnight the yellow crystals which formed were filtered off and washed with ether to give 112 mg (63%): mp 137–138° dec; ir, 6.07, 6.61, 9.0–9.3 μ; nmr, τ 2.1–3.0 (m, 2 OH), 5.81 (s, 2 H), 7.83 (s, 3 H).

Anal. Calcd for $C_{28}H_{25}N_2OP$: C, 77.06; H, 5.95; N, 6.42. Found: C, 76.63; H, 5.73; N, 6.72.

Attempted Synthesis of ω-Diazoacetophenone.—Acetophenone (240 mg, 2 mmol) was added to a suspension of 180 mg (4.5 mmol) of 60% NaH–oil in 3 ml of dry THF, and the mixture was stirred until all bubbling stopped. The reaction was cooled in an ice bath, and 394 mg (2 mmol) of tosyl azide was added. Work-up after 1 hr or overnight gave only starting materials.

Attempted Acid-Catalyzed Diazo Transfer.—Tosyl azide (1.10 g, 5.60 mmol) and 1.720 g (10 mmol) of *p*-toluenesulfonic acid were dissolved in ether, and 710 mg (3.60 mmol) of deoxybenzoin was added. After 18 hr work-up gave starting materials and no indication (ir, tlc) of diazodeoxybenzoin or of desyl tosylate.

Diazoacetone.—To a stirred solution of 80 mg (0.63 mmol) of 3-diazo-2,3-pentanedione in 2 ml of acetonitrile was added 3 ml of 1 *N* sodium hydroxide. After 1 hr the reaction was poured into water and extracted three times with small portions of methylene chloride. Evaporation of solvent gave 47 mg (90%) of product. Further treatment with base overnight did not effect further reaction: ir, 4.66, 6.07 μ; nmr ($CDCl_3$), τ 4.75 (s, 1 H), 7.89 (s, 3 H). The product was further characterized as the triphenylphosphine adduct, mp 137–139° (lit.[27] mp 141°).

(21) B. Eistert, H. Elias, E. Kosch, and R. Wollheim, *Chem. Ber.*, **92**, 130 (1959).
(22) H. Staudinger and G. Lüscher, *Helv. Chim. Acta*, **5**, 75 (1922).
(23) M. Regitz, *Chem. Ber.*, **99**, 3128 (1966).
(24) T. Curtius and H. Lang, *J. Prakt. Chem.*, **44** (2), 544 (1891).
(25) A. Kretov, *Ukr. Khim. Zh.*, **23**, 344 (1957); *Chem. Abstr.*, **52**, 4550 (1958).
(26) A. Adkins, W. Kutz, and D. Coffman, *J. Amer. Chem. Soc.*, **52**, 3112 (1930).
(27) H. Bestmann, H. Buckschweski, and H. Leube, *Chem. Ber.*, **92**, 1345 (1959).

Diazoacetophenone.—*p*-Carboxybenzenesulfonazide (260 mg, 1.10 mmol) was suspended in a stirred solution of 224 mg (1 mmol) of 1,3-diphenylpropane-1,3-dione (dibenzoylmethane) in 2 ml of acetonitrile. The mixture was cooled in an ice bath, and 303 mg (3 mmol) of triethylamine was added, upon which the azide went into solution. The reaction was brought to room temperature and stirred for 1 hr, and 1.5 ml of 1 *N* NaOH was added. After 18 hr the reaction was poured into water and extracted two times with methylene chloride yielding, from the organic layer, 151 mg of oil that solidified on standing. Crystallization from ether–petroleum ether gave 124 mg (85%) of diazoacetophenone: mp 47–49°; mmp 46–49° with authentic sample, prepared from benzoyl chloride and diazomethane; ir, 4.75, 6.17 μ; nmr ($CDCl_3$), τ 2.1–2.8 (m, 5 H), 4.02 (s, 1 H).

Ethyl Diazoacetate.—*p*-Carboxybenzenesulfonazide (131 mg 0.55 mmol) was suspended in a stirred solution of 72 mg (0.55 mmol) of ethyl acetoacetate in 1 ml of acetonitrile. The mixture was cooled in an ice bath, and 174 mg (1.73 mmol) of triethylamine was added, upon which the azide went into solution. The reaction was slowly warmed to room temperature, stirred for 2 hr, filtered, and stirred into 8 ml of 1 *N* NaOH. After 5 min the aqueous solution was extracted with methylene chloride, yielding 44 mg (69%) of a yellow oil: ir and nmr identical with those of distilled authentic ethyl diazoacetate (Aldrich)—ir, 4.73, 5.91 μ.

Hydrolysis of Diazodimedone.—To a solution of 70 mg (0.42 mmol) of diazodimedone in 3 ml of acetonitrile was added 2 ml of 1 *N* NaOH, and the mixture was stirred vigorously overnight. The reaction was poured into water, 2.5 ml of 1 *N* HCl was added, and the water was immediately extracted with methylene chloride. Evaporation of the organic layer gave 66 mg of a yellow oil whose spectra indicate it to be 6-diazo-5-oxo-3,3-dimethylhexanoic acid (84%): ir, 4.64, 5.86, 6.11 μ; nmr ($CDCl_3$), τ −1.13 (broad, 1 H), 4.56 (S, 1 H), 7.55 (s, 4 H), 8.86 (s, 6 H).

The presumed diazo acid (66 mg) was dissolved in ether and excess triphenylphosphine added. After 1 hr the reaction was filtered, and the precipitate was recrystallized from methylene chloride–ether to give 86 mg of an adduct, mp 144–146°, as white needles that give yellow solutions and turn brown on standing: ir, 4.73, 5.76, 6.31, 9.0, 9.2 μ; nmr ($CDCl_3$), τ −2.04 (broad, 1 H), 2.0–2.8 (m, 15 H), 7.29 (s, 2 H), 8.90 (s, 1.5 H), 9.20 (s, 4.5 H).

Reactions with Deoxybenzoin. A.—To a stirred solution of 373 mg (1.90 mmol) of deoxybenzoin in 8 ml of freshly distilled tetrahydrofuran was added 200 mg (5 mmol) of 60% NaH–oil. After 40 min the solution was cooled in an ice bath and 385 mg (1.93 mmol) of tosyl azide added. The reaction was brought to room temperature, stirred 15 min, filtered, poured into ether, and immediately extracted with water. Crystallization from ether–petroleum ether gave 238 mg (56%) reddish plates: mp 74–76°; mmp 74–77° with an authentic sample.[28] Acidification of the aqueous layer followed by extraction with methylene chloride gave 14 mg (2%) of N-tosyldiphenylacetamide, mp 178–180°.

B.—*p*-Carboxybenzenesulfonazide (240 mg, 1 mmol) was suspended in a stirred solution of 198 mg (1 mmol) of deoxybenzoin in 4 ml of acetonitrile and 303 mg (3 mmol) of triethylamine added, upon which the azide went into solution. The reaction was stirred overnight, poured into methylene chloride, and extracted with water. The aqueous layer was acidified, giving a fine white precipitate. Recrystallization from methylene chloride gave 295 mg (75%) of N-(*p*-carboxybenzenesulfonyl)-diphenylacetamide as a white powder: mp 231–233°; ir (KBr), 3.04, 5.89, 8.45, 9.23 μ; nmr (CD_3COCD_3), τ 1.82 (AB system, 4 H), 2.78 (s, 10 H), 4.81 (s, 1 H).

Anal. Calcd for $C_{21}H_{17}NO_5S$: C, 63.79; H, 4.30; N, 3.54; S, 8.10. Found: C, 63.45; H, 4.35; N, 3.88; S, 7.99.

Refluxing the imide for 4 hr in 50% HI gave, on cooling, a white precipitate which, after two recrystallizations from 50% ethanol, gave pure diphenylacetic acid: mp 141°; mmp 141–143° with authentic sample (Eastman).

C.—A solution of 1.96 g (10 mmol) of deoxybenzoin and 1.97 g (10 mmol) of tosyl azide in 20 ml of acetonitrile was stirred and cooled in a water bath, and 2.40 g (20 mmol) of triethylamine was added. The reaction mixture was stirred overnight, poured into methylene chloride, and extracted with water and 1 *M* H_2SO_4. Evaporation of the organic layer gave 1.90 g of white solid that recrystallized from benzene–petroleum ether to give 1.61 g, (44%) of N-tosyldiphenylacetamide as white needles: mp 180–181°; ir (KBr), 3.10, 5.82, 9.20 μ; nmr ($CDCl_3$), τ 2.8–3.1 (m, 14 H), 5.09 (s, 1 H), 7.56 (s, 3 H).

Anal. Calcd. for $C_{21}H_{19}HO_3S$: C, 69.12; H, 5.20; N, 3.84; S, 8.76. Found: C, 68.73; H, 5.27; N, 4.22; S, 8.85.

Further proof of structure was obtained by hydrolysis with 50% HI to diphenylacetic acid: mp 144–164°; mp 141–143° with authentic diphenylacetic acid (Eastman).

Reactions with Phenylacetone. A.—To a stirred solution of 134 mg (1 mmol) of 1-phenyl-2-propanone and 197 mg (1 mmol) of tosyl azide in 1 ml of acetonitrile was slowly added 2.3 mmol of triethylamine. After 24 hr the reaction mixture was poured into methylene chloride and extracted three times with water. Evaporation of the organic layer gave 206 mg of starting materials (ketone and azide). The aqueous layer was acidified and extracted three times with methylene chloride to give 92 mg (30%) of N-tosyl-2-phenylpropionamide: mp 140–142°; recrystallized from benzene–petroleum ether, mp 142–143° (lit.[29] mp 145°).

B.—To a stirred solution of 134 mg (1 mmol) of 1-phenyl-2-propanone in 5 ml of THF was slowly added 100 mg (2.5 mmol) of 60% NaH–oil. After 30 min the mixture was cooled in an ice–salt bath, and 197 mg (1 mmol) of tosyl azide was added. The reation mixture was stirred at room temperature for 15 min, filtered, poured into ether, and extracted three times with water. The aqueous layer was acidified and extracted with methylene chloride to give 11 mg (0.04 mmol, 4%) of N-tosyl-2-phenylpropionamide, mp 142–144°. The organic layer was crystallized from ether–petroleum ether to give 97 mg (0.61 mmol, 61%) of 1-diazo-1-phenyl-2-propanone: mp 55–57°; recrystallized from ether, mp 59–60° (lit.[29] mp 59–60°); ir, 4.82, 6.06 μ.

Reactions with 1,3-Diphenylacetone. A.—To a solution of 1.050 g (5 mmol) of 1,3-diphenylacetone and 0.985 g (5 mmol) of tosyl azide in 5 ml methylene chloride was slowly added 1.75 ml of triethylamine. The reaction mixture was stirred overnight and extracted three times with water and once with 1 *N* HCl. The organic layer was dried, and the methylene chloride was evaporated. The resulting oil was dissolved in a small amount of ether and shaken with 1 *N* NaOH, upon which a fluffy precipitate was formed. Filtration and recrystallization of the white solid from acetone gave 880 mg (46%) of the sodium salt of N-tosyl-1,2-diphenylpropionamide, mp *ca.* 310°.

Anal. Calcd for $C_{22}H_{20}NO_3SNa$: C, 65.83; H, 4.99; N, 3.49; S, 7.98. Found: C, 66.0; H, 4.92; N, 3.57; S, 8.19.

Shaking a methylene chloride solution of the salt with dilute acid gave the free imide, which could not be obtained crystalline: ir, 2.96, 5.78, 7.12, 8.67, 9.36 μ; nmr ($CDCl_3$), τ 2.2–3.4 (m, 14 H), 6.1–7.4 (m, 3 H), 7.58 (s, 3 H).

B.—To a stirred suspension of 100 mg (2.5 mmol) of 60% NaH–oil in 5 ml of tetrahydrofuran was added 210 mg (1 mmol) of 1,3-diphenylacetone. The mixture was stirred for 15 min and cooled in an ice bath, and 197 mg (1 mmol) of tosyl azide was added. After 2 hr the reaction was filtered, poured into water, and worked up to give 196 mg (52%) of the above imide. No evidence (ir spectra) of diazo ketone was found in either procedure.

Reaction of Phenylacetaldehyde.—To a stirred solution of 120 mg (1 mmol) of phenylacetaldehyde and 197 mg (1 mmol) of tosyl azide in 2 ml of acetonitrile was added 2.5 mmol of triethylamine, upon which the solution slowly bubbled. After 18 hr the reaction was poured into methylene chloride and extracted with 0.1 *N* HCl. Evaporation of the organic layer gave 156 mg (54%) of N-tosylphenylacetamide, recrystallized from 80% ethanol to 133 mg (46%), mp 145.5–147.5° (lit.[30] mp 149°).

Reaction of 1,1-Diphenylacetone.—To a stirred suspension of 100 mg (2.5 mmol) of 60% NaH–oil in 5 ml of THF was added 210 mg (1 mmol) of 1,1-diphenylacetone. After all bubbling had stopped, 197 mg (1 mmol) of tosyl azide was added. The reaction was stirred overnight, when an ir spectra of the reaction mixture showed no starting material but did show a diazo peak at 4.89 μ. The reaction was poured into ether, extracted with water, dried, and added to an ethereal solution of 250 mg of benzoic acid. After all bubbling had stopped, the solution was extracted with 1 *N* NaOH and chromatographed on silica, giving 66 mg (0.23 mmol, 23%) of benzhydrol benzoate, mp 86–87° (lit.[31] mp 87°), and 30 mg (15%) of slightly impure benzophenone, identified by ir, nmr, and uv spectra and tlc

(28) H. Staudinger and J. Siegwart, *Ber.*, **49**, 1918 (1916).

(29) M. Regitz, *ibid.*, **98**, 1201 (1965).

(30) A. Rarkovas-Prpic and N. Tipic, *Croat. Chem. Acta*, **35**, 263 (1963); *Chem. Abstr.*, **60**, 13175 (1964).

(31) E. Linnemann, *Ann.*, **133**, 1 (1865).

comparison with authentic material. Acidification of the initial aqueous layer followed by extraction with methylene chloride and crystallization of the organic layer from 95% ethanol gave 48 mg (22%) of N-tosylacetamide, mp 134–136° (lit.[25] mp 137°). Using triethylamine as the base gave only partial reaction; work-up after 4 days gave back *ca.* 55% of starting materials.

Reaction of Diphenylacetaldehyde.—To a stirred suspension of 100 mg (2.5 mmol) of 60% NaH–oil in 5 ml of THF was added 197 mg (1 mmol) of tosyl azide. The mixture was cooled in an ice bath, and 196 mg (mmol) of diphenylacetaldehyde in 5 ml of THF was added slowly. The red reaction was stirred at room temperature for 15 min and filtered, ether was added, and the solution was filtered again. The ether solution was extracted with water, dried, and added to a solution of 150 mg of benzoic acid in ether. After 30 min the mixture was chromatographed on silica to give 82 mg (29%) of benzhydrol benzoate, mp 86–87° (lit.[31] mp 87°), and 32 mg (15%) of impure benzophenone (see above). The precipitate obtained by the second filtration (after the addition of ether) was dissolved in water; the solution was made acid with concentrated HCl, extracted with methylene chloride, and dried. Evaporation gave 167 mg (46%) of N-tosyldiphenylacetamide: mp 178–180°; mmp 177–179° with authentic sample (above). Using triethylamine, the reaction would not go to completion (2 days), and, although ketone and amide were identified, no diazo compound was produced (ir spectra).

2-Phenylpropionaldehyde. N-Tosyl-2-phenylpropionamide. A.—To a stirred solution of 134 mg (1 mmol) of 2-phenylpropionaldehyde and 197 mg (1 mmol) of tosyl azide in 2 ml of acetonitrile, 2.5 mmol of triethylamine was added. After 18 hr the reaction was poured into water and extracted with methylene chloride, and the organic layer was back-extracted with dilute acid. Evaporation of the methylene chloride followed by crystallization from benzene–petroleum ether gave 91 mg (28%) of N-tosyl-2-phenylpropionamide, mp 133–134°. Examination of the mother liquors revealed considerable starting material. Further crystallization of the imide from methylene chloride–petroleum ether gave mp 144–145° (lit.[29] mp 145°).

Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.66; N, 4.62; S, 10.56. Found: C, 63.34; H, 5.67; N, 4.64; S, 10.47.

B.—A stirred solution of 134 mg (1 mmol) of 2-phenylpropionaldehyde and 197 mg (1 mmol) of tosyl azide in 2 ml of acetonitrile was cooled in an ice bath, and 2 mmol of diethylamine was added. After 1.5 hr the reaction was poured into water and extracted with methylene chloride. Acidification of the water layer followed by extraction with methylene chloride gave 72 mg (0.24 mmol, 24%) of N-tosyl-2-phenylpropionamide, identical with authentic material prepared above. The organic layer showed the presence of a diazo compound (ir, 4.90 μ; estimated yield, 20%), but addition of triphenylphosphine to an ethereal solution did not give a precipitate, and ir spectra showed that no adduct had formed. Addition of the organic layer to acidic 2,3-dinitrophenylhydrazine solution in ethanol gave violent bubbling, followed by precipitation of 98 mg (31%) of acetophenone 2,4-dinitrophenylhydrazone, mp 245–246° (lit.[32] mp 250°).

Preparation of Other Diazo Transfer Reagents. A. N,N-Dimethylsulfamoyl Azide.—N,N-Dimethylsulfamoyl chloride was prepared by a modification of the method of Behrend.[33] Dimethylamine hydrochloride (11.5 g, 0.14 mol) was added to 100 ml of sulfuryl chloride, and the mixture was gently refluxed for 40 hr. The sulfuryl chloride was boiled off, and the product was distilled at 48° (0.5 mm) [lit. 67° (8 mm)] to give 12.30 g (61%) of product: ir, 6.93, 7.3, 8.6, 9.6 μ. The chloride was dissolved in ethanol, and 24.6 g of sodium azide in water was slowly added. After 1 hr the reaction was poured into water and extracted with methylene chloride. Evaporation of the organic layer gave 11.3 g (53%) of product, an oil that gave a negative chloride test and decomposed on heating: ir, 4.70, 7.3, 8.4, 8.7, 10.4 μ.

B. *o*-Benzenedisulfonyl Azide Chloride.—A stirred solution of 137 mg (0.5 mmol) of *o*-benzenedisulfonyl chloride in methylene chloride was cooled in an ice bath, and 142 mg (0.5 mmol) of tetrabutylammonium azide (prepared by aqueous ion exchange from the iodide) in methylene chloride was slowly added. After 30 min, the reaction was extracted with water, and the organic layer was evaporated to give a white powder, recrystallized from petroleum ether to give 99 mg of white needles, mp 122–124° dec. Tlc showed this to be mostly one compound with a small amount of *o*-benzenedisulfonyl chloride as an impurity. As further recrystallization or chromatography did not remove the impurity, the azide–chloride was used in further reactions in this state: ir, 4.62, 8.4, 8.5 μ.

Anal. Calcd for $C_6H_4N_3S_2ClO_4$ (281.5): C, 25.58; H, 1.42; S, 22.77; N, 14.85; Cl, 12.63. Found: C, 25.56; H, 1.63; S, 22.72; N, 12.32; Cl, 14.10.

Diazo Transfer with Other Reagents. A.—To a solution of 320 mg (2.28 mmol) of dimedone and 360 mg (2.40 mmol) of N,N-dimethylsulfamoyl azide in 10 ml of ether was added 460 mg (4.60 mmol) of triethylamine. After 18 hr the reaction mixture was poured into 500 ml of 0.02 *N* HCl and extracted with methylene chloride. Evaporation of the organic layer followed by two crystallizations from petroleum ether gave 229 mg (61%) of diazodimedone, mp 106–107°.

B.—A stirred solution of 75 mg (0.58 mmol) of ethyl acetoacetate and 175 mg (0.62 mmol) of *p*-benzenedisulfonyl azide chloride in methylene chloride was cooled in an ice bath, and 130 mg (1.3 mmol) of triethylamine was added. The reaction mixture was stirred for 1 hr and then extracted with water. The organic layer yielded only 59 mg of an oil which proved (ir and nmr spectra, tlc) to be a mixture of starting ester, diazo compound, and sulfonyl-containing material; the aqueous layer afforded no sulfonimide on evaporation.

In another experiment, 9 mg (0.07 mmol) of ethyl acetoacetate and 19 mg (0.09 mmol) of azide chloride were allowed to react with 15 mg of 60% NaH–oil in tetrahydrofuran with stirring for 45 min and then filtered. Ir spectra inspection of the organic layer showed roughly equal amounts of diazo ester, and starting ester whereas with tosyl azide under these conditions the ir spectra showed only diazo compound and no starting material. The reaction mixture also showed only the slow precipitation with silver nitrate characteristic of sulfonyl chloride rather than the rapid reaction of ionic chloride.

C.—A stirred solution of 65 mg (0.5 mmol) of ethyl acetoacetate and 127 mg (0.5 mmol) of picryl azide[34] in 2 ml of methylene chloride was cooled in an ice bath, and 2.5 mmol of triethylamine was added. After 90 min the reaction was poured into ether and extracted six times with 1 *N* hydroxide and once with water. Evaporation of solvent gave 65 mg of a mixture (oil and solid) that ir spectral analysis indicated to be *ca.* 80% ethyl diazoacetoacetate (66% yield) and 20% picryl amide, by comparison with authentic mixtures.

D.—*p*-Nitrobenzenesulfonyl azide[35] was compared with tosyl azide in an early experiment in which 490 mg (2.50 mmol) of desoxybenzoin and 3.50 mmol of each azide were separately allowed to react with 3 mmol of sodium methoxide in methanol for 5 min, then poured into pentane, filtered, and washed with water. In the case of tosyl azide, crystallization from the organic layer afforded 48% red-orange crystals of diazo ketone, mp 74–76°, whereas with the nitro azide, crystallization could not be effected and quantitative comparison of the ir spectrum with those of known mixtures showed only 20% diazodesoxybenzoin to be present as well as substantial starting material.

E.—In a 0.5-hr reaction otherwise comparable with those in D above methanesulfonyl azide[36] produced no ir spectral evidence of diazodesoxybenzoin.

Ethyl Nitrodiazoacetate.—To a stirred solution of 133 mg (1 mmol) of ethyl nitroacetate[37] in 2 ml of acetonitrile was added 240 mg (1 mmol) of *p*-carboxybenzenesulfonazide. Upon the addition of 0.3 ml of pyridine to this mixture, the azide slowly went into solution. After 18 hr the reaction mixture was poured into ether, extracted with base, and filtered through a plug of silica gel to give 13 mg (8%) of product as a yellow oil: ir, 4.68 5.78, 6.68 μ. The oil was dissolved in ether, and excess triphenylphosphine was added. Refrigeration and addition of petroleum ether gave a solid which, on repeated recrystallization, melted at 134–135° (lit.[38] mp 133–134°).

(32) R. Shriner, R. Fuson, and D. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p 317.

(33) R. Behrend, *Ann.*, **222**, 116 (1884).

(34) A. Korczynski and S. Mamyslowski, *Bull. Soc. Chim. Fr.*, **35**, 1186 (1924).

(35) L. Horner and A. Christmann, *Chem. Ber.*, **96**, 388 (1963).

(36) J. H. Boyer, C. H. Mack, N. Goebel, and L. R. Morgan, Jr., *J. Org. Chem.*, **23**, 1051 (1958).

(37) W. Davey and D. Tivey, *J. Chem. Soc.*, 2276 (1958).

(38) (a) U. Schöllkopf and P. Markush, *Tetrahedron Lett.*, 6199 (1966); (b) U. Schöllkopf and H. Schafer, *Angew. Chem. Intern. Ed. Engl.*, **4**, 358 (1965).

3-Azo-2-methylindole.—To a stirred suspension of 100 mg (2.5 mmol) of 60% NaH–oil in 5 ml of THF was added 131 mg (1 mmol) of 2-methylindole. After all bubbling had ceased, the solution was cooled in an ice bath and 197 mg (1 mmol) of tosyl azide added. After 5 min the reaction was filtered, poured into methylene chloride, and filtered again. The second filtrate consisted of 68 mg of yellow powder, mp 293–297° dec, which was insoluble in methylene chloride and slightly soluble in ether and acetone. Mass spectra (molecular weight 288, fragmentation pattern similar to starting material) and nmr spectra [similar to starting material but lacking the τ 3.83 peak (H at C-3)] indicate that this is 3-azo-2-methylindole (yield 43%). The methylene chloride solution showed no diazo compound (ir spectra), and on work-up gave 36 mg (27%) of starting indole.

2-Carbethoxy-5-methoxyindole.—To a stirred suspension of 100 mg (2.5 mmol) of 60% NaH–oil in 5 ml of THF was added 245 mg (1 mmol) of 2-carbethoxy-5-methoxyindole. After all bubbling had stopped, the solution was cooled in an ice bath, and 394 mg (2 mmol) of tosyl azide was added. After 5 min the reaction turned black. Work-up at this point or after stirring overnight gave only starting material.

3-Diazo-2-phenylindole.—To a stirred suspension of 200 mg (5 mmol) of 60% NaH–oil in 15 ml of THF was added 348 mg (2 mmol) of 2-phenylindole. After all bubbling had stopped, the solution was cooled in an ice bath, and 788 mg (4 mmol) of tosyl azide was added all at once. The reaction was immediately filtered, and the precipitate was washed several times with THF. The combined THF layers were poured into ether and extracted four times with 0.1 *N* HCl. The aqueous solution was made basic with hydroxide and extracted with methylene chloride. Evaporation of solvent gave 362 mg (83%) of 3-diazo-2-phenylindole: mp 104.5–106° (lit.[39] mp 107°); ir, 4.73 μ. Dissolving the diazo compound in ether and bubbling in dry HCl gas gave a precipitate of 3-diazo-2-phenylindole hydrochloride: mp 173–174° (lit.[40] mp 173–175°); ir, 4.63 μ. If the reaction is allowed to proceed for 2 min, work-up and crystallization from methylene chloride–petroleum ether gives 20 mg (0.046 mmol, 4.6%) of 3-azo-2-phenylindole as blood red plates, mp 260° dec (lit.[41] mp 263° dec).

Diazomethane.—A freshly prepared solution of 3 mmol of methylmagnesium iodide in ether was cooled in a Dry Ice–acetone bath, and 632 mg (3.2 mmol) of tosyl azide was added. The reaction was slowly warmed to ice-bath temperature, and 4 mmol of benzoic acid was added. After 2 hr the reaction mixture was evaporated and chromatographed on silica to give 360 mg (1.8 mmol) of tosyl azide and 30 mg (0.22 mmol, 7%) of methyl benzoate, ir spectra and the identical with those of an authentic sample.

Phenyldiazonium Salt and Decomposition.—A stirred solution of 1.182 g (6 mmol) of tosyl azide in 10 ml of toluene was cooled in a Dry Ice–acetone bath, and 3.6 mmol of freshly prepared phenylmagnesium bromide in 20 ml of ether was added slowly. The reaction was stirred for 5 min and brought to room temperature, excess BHF_4–water was added, and the entire reaction mixture was refluxed for 3 hr. The aqueous layer was separated and extracted six times with methylene chloride. The two organic layers were combined and chromatographed, giving 117 mg (35%) of phenol (mp 37–40°; ir and tlc identical with those of authentic material), 146 mg (26% based on tosyl azide, 52% based on phenylmagnesium bromide) of biphenyl (mp 69–70°; mmp 68–70° with an authentic sample; ir spectra and tlc identical with those of an authentic sample), 343 mg (56%) of tosyl amide, and 751 mg (3.80 mmol) of unreacted tosyl azide.

Attempted Synthesis of Diazoacetophenone Trichlorophosphorazine. α-Chloroacetophenone.—To a solution of 258 mg (1.70 mmol) of diazoacetophenone in ether was added 273 mg (2 mmol) of phosphorus trichloride. The solution immediately bubbled and lost its yellow color. After 18 hr the reaction was extracted with water and evaporated to give 151 mg (58%) of a lacrimatory oil, which slowly gives a precipitate with silver nitrate and has an ir spectrum and tlc identical with those of authentic α-chloroacetophenone.

Attempted Decompositions of Diazoacetophenone Triphenylphosphorazine. A.—The phosphorazine[42] (24 mg) was suspended in 1 ml of glacial acetic acid, and the mixture was warmed to 65°, when the adduct went into solution. After 90 min of heating, the dark red reaction mixture was poured into ether and extracted with bicarbonate and water. Evaporation of the organic layer gave 20 mg of a dark solid. Tlc indicates the presence of starting material and triphenylphosphine, but showed no α-acetoxyacetophenone (made by warming diazoacetophenone in glacial acetic acid[43]).

B.—The phosphorazine (19 mg) was suspended in 0.5 ml of glacial acetic acid and 2 drops of freshly distilled boron trifluoride ethereate was added, upon which the adduct went into solution. After standing overnight the dark red solution was worked up as above to give 19 mg of oil. Tlc showed the presence of starting material and triphenylphosphine but indicated no α-acetoxyacetophenone.

Attempted Decomposition of Diazodesoxybenzoin Triphenylphosphorazine.—The phosphorazine (483 mg, 1 mmol) and 60 mg (1 mmol) of acetic acid were dissolved in 5 ml of methylene chloride, and several drops of freshly distilled boron trifluoride etherate was added. The reaction was refluxed for 6 hr, left stand overnight, filtered, and extracted with water. Evaporation of the organic layer gave 524 mg of orange tar. Crystallization from chloroform–ether gave 95 mg (0.23 mmol, 23%) of bisbenzilketazine, mp 205° (lit.[44] mp 202). No other product was isolated; tlc and ir spectra of the mother liquor indicated the absence of benzoin acetate and the presence of more ketazine.

Cyclohexyl Azide.—To a solution of 3 mmol of methylmagnesium iodide in ether was added 248 mg (2.50 mmol) of cyclohexylamine. This solution was then slowly added to a stirred, ice bath cooled solution of 790 mg (4.00 mmol) of tosyl azide in 5 ml of tetrahydrofuran. After 1 hr the reaction mixture was filtered, concentrated, and chromatographed on silica gel, yielding 141 mg (45%) of cyclohexyl azide as an oil (ir, 4.78 μ), one spot tlc, bp 160° (lit.[45] bp 158°).

Other Azides.—Using the same procedure, other azides were made as follows. In no case did the free amine or catalysis by sodium hydride or triethylamine as in the procedures above afford an azide product.

A.—Phenyl azide from aniline yields an oil (47%) identical with authentic material[46] by tlc and ir spectral comparison.

B.—*n*-Butyl azide from *n*-butylamine yields (using 8.0 mmol of tosyl azide) an oil (24%), bp 108° (lit.[47] bp 106.5°).

C.—Benzyl azide from benzylamine yields (using 8.0 mmol of tosyl azide) an oil (23%) identical with authentic material[48] by tlc and ir spectral comparison.

D.—N-Benzylacetamide under the same conditions yields only starting materials.

Registry No.—*p*-Carboxybenzenesulfonazide, 17202-49-2; ethyl α-diazopropionate, 17202-50-5; triphenylphosphine adduct with ethyl α-diazopropionate, 17203-27-9; 4-phenyl-3-diazo-2-butanone, 17203-28-0; triphenylphosphine adduct with 4-phenyl-3-diazo-2-butanone, 17203-29-1; 6-diazo-5-oxo-3,3-dimethylhexanoic acid, 17203-30-4; triphenylphosphine adduct with 6-diazo-5-oxo-3,3-dimethylhexanoic acid, 17203-31-5; N-(*p*-carboxybenzenesulfonyl)diphenylacetamide, 17203-32-6; N-tosyldiphenylacetamide, 3864-27-5; sodium salt of N-tosyl-1,2-diphenylpropionamide, 17203-34-8; *o*-benzenedisulfonyl azide chloride, 17203-35-9.

Acknowledgment.—The work reported here was part of a continuing study of sulfonyl compounds as synthetic reagents, generously supported by National Science Foundation Grant GP-5525, for which we wish to express our gratitude.

(39) H. Patel and J. Tedder, *J. Chem. Soc.*, 4593 (1963).
(40) V. Castella and A. D'Angelo, *Gazz. Chim. Ital.*, **36** II, 56 (1906).
(41) S. Capuano, *Atti Congr. Intern. Chim. 10°, Rome, 1938*, **3**, 73 (1939); *Chem. Abstr.*, **34**, 1015 (1940).
(42) G. Mäkl, *Tetrahedron Lett.*, 811 (1961).
(43) W. Bradley and R. Robinson, *J. Chem. Soc.*, 1310 (1928).
(44) J. Ritter and G. Wiedmann, *J. Amer. Chem. Soc.*, **51**, 3583 (1929).
(45) E. Lieber, C. N. Ramachandra Rao, T. S. Chao, and W. H. Wahl, *J. Sci. Ind. Res.*, **16B**, 95 (1957); *Chem. Abstr.*, **51**, 13808 (1957).
(46) J. Horwitz and V. Grakauskas, *J. Amer. Chem. Soc.*, **80**, 926 (1958).
(47) J. Boyer and J. Hamer, *ibid.*, **77**, 951 (1955).
(48) T. Curtius and G. Ehrhart, *Chem. Ber.*, **55**, 1559 (1922).