

PREPARATION OF α -DIAZO CARBONYL COMPOUNDS

Michael Rosenberger and Peter Yates*

Department of Chemistry, University of Toronto
Toronto 5, Ontario, Canada

and

James B. Hendrickson[†] and Walter Wolf

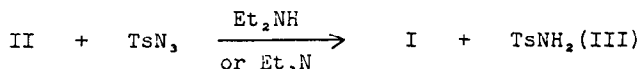
Department of Chemistry, Brandeis University, Waltham 54, Mass.

(Received 17 June 1964)

The rational synthesis of diazocyclopentadiene by the reaction of cyclopentadienyllithium with tosyl azide designed by Doering and De Puy(1) more than a decade ago has only recently been extended to the preparation of other diazo compounds(2,3,4,5). Regitz(4,5) has reported its application to the synthesis of α -diazo carbonyl compounds and we now give a preliminary account of our investigations, which complement and extend his observations.

Three methods have been developed for the preparation of a diazo carbonyl compound $\text{RCOCN}_2\text{R}'$ (I) from a compound $\text{RCOCH}_2\text{R}'$ (II):

A. Reaction of II in diethyl ether with tosyl azide and diethylamine (cf. 2) or triethylamine:



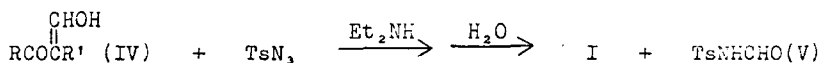
*Hoffmann-La Roche Fellow

[†]Alfred P. Sloan Research Fellow

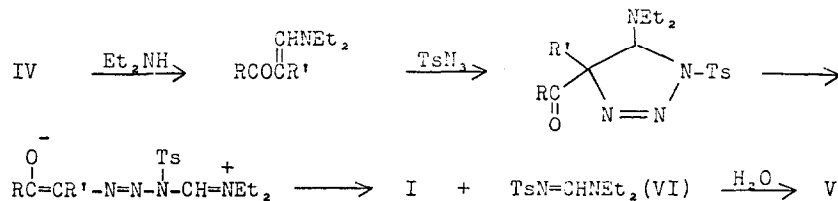
This method was found to be effective with β -dicarbonyl compounds(II, R' = COR''); it differs from the previously reported method(4,5) in the use of alkylamines as condensing agents in place of the more strongly basic potassium ethoxide.

B. Reaction of II in *t*-butyl alcohol with tosyl azide and potassium *t*-butoxide. This method resembles that of Regitz(4,5) in the use of strongly basic conditions.

C. Conversion of II to the corresponding hydroxymethylene derivative IV and reaction of this in diethyl ether with tosyl azide and diethylamine, followed by addition of the reaction mixture to water:

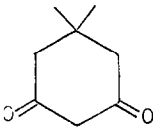
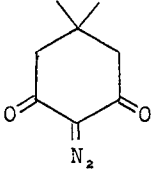
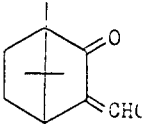
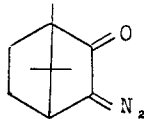
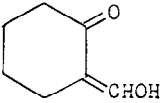
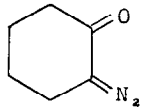


This method was found to be effective for the preparation of diazo ketones from simple ketones. It represents a useful extension of the general method, which has only been used heretofore for the preparation of diazo ketones from compounds in which the methylene group is activated by both a carbonyl group and an aromatic ring(4) or by two carbonyl groups(5). It is considered to involve the following route:



The amide V, m.p. 103-104°(lit.(6) m.p. 103.5°) was characterized by its hydrolysis to III. When the contact time of the reaction mixture with water was reduced, there was isolated in

TABLE

Compound	Method	Product (Yield)	Identification ^a
$\text{CH}_3\text{COCH}_2\text{CO}_2\text{Et}$	A ^b	$\text{CH}_3\text{COCN}_2\text{CO}_2\text{Et}$ (80%) b.p. 84-85° (5 mm.)	IR comparison with authentic sample(8)
$\text{CH}_2(\text{CO}_2\text{Et})_2$	A ^b	$\text{CN}_2(\text{CO}_2\text{Et})_2$ (75%) b.p. 73-75° (0.7 mm.)	As $^+\text{NH}_3\text{CH}(\text{CO}_2\text{Et})_2 \text{Br}^-$ m.p. 161-163° (lit.(9)) m.p. 162-163°
	A ^c	 (78%) m.p. 107-109°	Lit.(10) m.p. 106-108°
	C	 (74%) m.p. 69-72°	IR comparison with authentic sample(11), m.p. 74-75°
	C	 (83%) ^d b.p. 35° (0.05 μ)	Conversion by boiling <u>N</u> -methylaniline to <u>N</u> -methylcyclopentane-carboxanilide, ^e m.p. 132°
$\text{C}_6\text{H}_5\text{COCH}_2\text{C}_6\text{H}_5$	B	$\text{C}_6\text{H}_5\text{COCN}_2\text{C}_6\text{H}_5$ (50%) m.p. 76-77°	Lit.(12) m.p. <u>ca.</u> 79°

^aAll products had IR and NMR spectra in accord with expectation

^bWith diethylamine ^cWith triethylamine

^dYield of crude product with IR spectrum identical to that of distilled material

^eFound: C, 76.67; H, 8.41; N, 7.04%

addition to I and V a compound, $C_{12}H_{18}N_2O_2S$, m.p. 74-76° (Found: C, 56.31; H, 7.26; N, 10.96; S, 12.55%), which was converted to V on mild hydrolysis. On the basis of these data and its IR and NMR spectra it is assigned structure VI.

The diazo carbonyl compounds prepared are listed in the Table. The following are typical procedures:

(i) A solution of ethyl acetoacetate (2.61 g., 0.0200 mole) and tosyl azide (3.94 g., 0.0200 mole) in diethyl ether (20 ml.) at 0° was treated with diethylamine (2 ml., 0.020 mole). The mixture was stirred for 15 min. at 0° and for a further 30 min. at room temperature, when a solid was deposited. The mixture was treated with *n*-pentane (150 ml.) and was filtered to give III, m.p. 125-126° (authentic sample m.p. 125-126° (3.2 g., 94%). Removal of solvent from the filtrate and distillation of the residue gave ethyl acetodiazooacetate, b.p. 84.5-85° (5 mm.) (2.52 g., 80%).

(ii) A solution of 2-hydroxymethylenecyclohexanone (7) (5.0 g., 0.040 mole) and tosyl azide (7.8 g., 0.040 mole) in diethyl ether (100 ml.) at 10° was treated with diethylamine (5.8 g., 0.080 mole). The mixture was stirred at room temperature for 45 min., poured into water and extracted with ether. Removal of the solvent from the dried ethereal extract gave 2-diazocyclohexanone (4.1 g., 83%). Distillation of a portion of this product at 35° (0.05 μ) gave an oil with unchanged IR spectrum: bands (CCl_4) at 4.78, 6.11, 7.41 μ .

We acknowledge with gratitude support by the Roche Anniversary Foundation, the Alfred P. Sloan Foundation, and the National Research Council of Canada.

REFERENCES

- (1) W. von E. Doering and C. H. De Puy, J. Am. Chem. Soc. 75, 5955 (1953).
- (2) T. Weil and M. Cais, J. Org. Chem. 28, 2472 (1963).
- (3) F. Klages and K. Bott, Chem. Ber. 97, 735 (1964).
- (4) M. Regitz, Tetrahedron Letters, 1403 (1964).
- (5) M. Regitz and G. Heck, Chem. Ber. 97, 1482 (1964).
- (6) S. I. Burmistrov and G. E. Krakovtseva, Ukrain. Khim. Zhur. 24, 348 (1958) (C.A. 53, 1219 (1959)).
- (7) C. Ainsworth, Org. Syntheses Coll. Vol. 4, 536 (1963).
- (8) L. Wolff, P. Bock, G. Lorentz and P. Trappe, Ann. 325, 134 (1902).
- (9) W. von E. Doering and L. H. Knox, J. Am. Chem. Soc. 83, 1989 (1961).
- (10) B. Eistert, H. Elias, E. Kosch and R. Wollheim, Chem. Ber. 92, 130 (1959).
- (11) P. Yates, H. Morrison and S. Danishefsky, J. Org. Chem. 26, 2617 (1961).
- (12) C. D. Nenitzescu and E. Solomonica, Org. Syntheses Coll. Vol. 2, 496 (1943).