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CATALYZED INSERTION REACTIONS OF SUBSTITUTED α-DIAZOESTERS. A NEW SYNTHESIS OF CIS-ENOATES[1]

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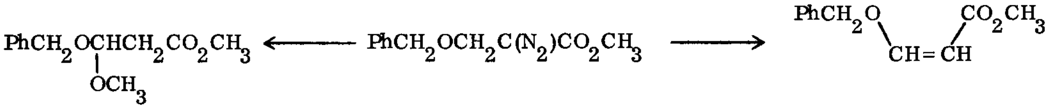
Summary: The decomposition of α-diazoesters is notably catalyst-dependent; with rhodium (II) carboxylates a stereoselective insertion reaction leads to the title structures in high yield.

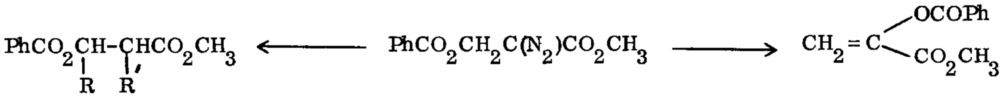
The insertion of organic diazo compounds into acidic X-H bonds, catalyzed by a variety of acids[3] and transition metals,[4] has long constituted a powerful synthetic method for heteroatom alkylation.[5] Alpha-diazoesters have been used to effect difficult O-alkylations at neutral pH[6a] and to construct highly strained ring systems by NH insertion.[6b] The stereoselective formation of cis and trans-cinnamates from diazotized phenylalanine derivatives has also been reported.[7] Recently Pellicciari et al. described the $Rh(OAc)_2$-induced conversion of α-diazo-β-hydroxyesters to β-ketoesters in high yield.[8] Our own interest since 1977 in the preparation of biologically important pyruvic acid enol ethers[9] led us to discover this same process while exploring the catalyzed insertion chemistry of various functionalized α-diazoesters. Other new rearrangements we have noted now make possible some generally useful synthetic methods which are the subject of this Letter.

When methyl benzyloxy-α-diazopropionate 1[10] was treated with methanol (1 equiv) and a trace of HBF_4(CH_2Cl_2, 0°, 2h), N_2 was evolved and acetal 2 was produced in 54% yield [NMR δ ($CDCl_3$) 5.01 (t, 1H, J=6 Hz), 4.62 (m, 2H), 3.69, 3.37 (2s, 3 H each), 2.7 (d, 1H, J=6 Hz)]. In contrast, 1 afforded exclusively cis-3 upon exposure to a catalytic quantity of $Rh(OAc)_2$ in benzene [rt, 1h, 90%; NMR δ ($CDCl_3$) 6.41, 5.75 (AB quartet, 2H, J=6 Hz)]. We could not ascertain whether enol ether 3 was an intermediate in the HBF_4-catalyzed formation of 2, or if the mixed acetal arose directly from 1 by protonation and hydride migration. The rapid conversion of 1 to a mixture of 2 and 3 (1 : 1, 80%) using $Rh(OAc)_2$ in CH_3OH clearly demonstrated the susceptibility of 3 to alcoholysis under very mild conditions.[11]



2 1 3

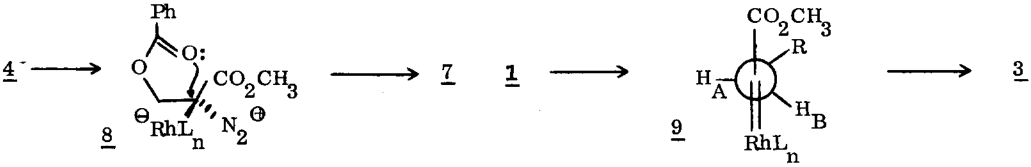
To test the hydride transfer mechanism, methyl benzoyloxy-α-diazopropionate 4 was synthesized from N-Cbz-O-benzoylserine methyl ester. In CH_3OH-CH_2Cl_2 containing HBF_4, 4 slowly decomposed to afford a 4 : 1 mixture of 5 and 6 (36%). The major product was conclusively identified as α-methoxy ester 5 by DBU elimination ($CHCl_3$, rt) to methyl α-methoxyacrylate. This outcome was consistent with protonation of 4 to an intermediate diazonium ion and partitioning between direct alcohol coupling and H-shift pathways. In contrast, treatment of 4 with $Rh(OAc)_2$ ($CDCl_3$, rt, 30 min) furnished only the rearranged α-benzoyloxyacrylate 7 [94%; NMR δ ($CDCl_3$) 6.10, 5.55 (AB quartet, 2H, J=2Hz)].



4 7

5 R = H, R' = OCH_3
6 R = OCH_3, R' = H

Metal-stabilized carbenoids possessing electrophilic character may be responsible for the unusual rhodium acetate-catalyzed reactions of 1 and 4, and one plausible mechanistic picture is presented below.



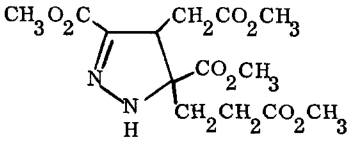
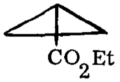
In the case of 4, carbonyl participation through a 5-membered cyclic array as in 8 (or its derived metal carbene) can lead to 7 by benzoate migration. The fate of 1 can also be rationalized by such a species 9 wherein migration of H_A furnishes 3 as a single isomer.[12] This interpretation suggests a general synthetic access to cis-disubstituted enoates which has now been realized (see

Table). The decomposition of glutamate derivative 12 was concentration dependent and generally afforded the desired cis-dimethylglutaconate [NMR δ ($CDCl_3$) 5.90, 6.65 (J_{vinyl} = 11 Hz)] in disappointing yield. Formation of dimer 13 [mp 67-68°, m/e (CI) 345 (M^+, 100%)] could be supressed by dilution, whereupon 12 afforded predominantly dimethyl α-hydroxyglutarate, perhaps reflecting γ-carbomethoxy participation as in 8. Besides the expected cis-vinylacrylate 15, diazopentenoic ester 14 also furnished ethyl bicyclobutane-1-carboxylate 16 in a remarkable reaction. Although strained ring structures undergo rearrangements catalyzed by various Rh^I and Pd^{II} complexes, 16 proved stable towards $Rh(OAc)_2$ and $Rh(OCOCF_3)_2$ for prolonged periods even at 80° in benzene.[13] Isoleucine derivative 17 decomposed essentially nonstereoselectively to an E-Z mixture of trisubstituted olefin 18 in high yield.

The overall deamination of α-aminoesters, which are readily accessible by straightforward alkylation routes,[14] represents an efficient laboratory mimic of the biologically important ammonia lyase enzymes.[15]

TABLE

Cis-Enoates from $Rh(OAc)_2$-Catalyzed α-Diazoester Decomposition[a]

Diazoester		Product		Yield	(Ref)
1		3		90%	
$(CH_3)_2CHCH_2C(N_2)CO_2CH_3$	10	cis-$(CH_3)_2CHCH{=}CHCO_2CH_3$		99%	(16)
$PhCH_2C(N_2)CO_2CH_3$	11	cis-methyl cinnamate		100%	(7)
$CH_3O_2CCH_2CH_2C(N_2)CO_2CH_3$	12	cis- dimethyl glutaconate dimethyl α-hydroxyglutarate		14% 44%[b]	
		 13		62%[c]	
$CH_2{=}CHCH_2C(N_2)CO_2Et$	14	cis-$CH_2{=}CH{-}CH{=}CHCO_2Et$	15	39%	(17)
			16	51%	(18)
$CH_3CH_2(CH_3)CHC(N_2)CO_2CH_3$	17	$CH_3CH_2(CH_3)C{=}CHCO_2CH_3$ E : Z 57 : 43	18	95%	(19)

(a) To a solution of each diazoester in benzene (.1-.5M) was added a trace (1-2 mg) of

$Rh(OAc)_2$ (Strem Chemical Co.). Immediate gas evolution was noted and after 30 min the solution was filtered through a short plug of 30-60μ silica gel using $CHCl_3$. Concentration at reduced pressure afforded the pure enoates whose IR and NMR matched the published spectra of authentic samples. (b) From a reaction at 0.019M; purified by flash chromatography. (c) From a reaction at 0.51M; recrystallized from ether-hexane.

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(11) We have additionally prepared α-diazo-β-hydroxypropionic esters i both by reducing dimethyl diazomalonate with DIBAL-H (hexane, -78°) and by condensing ethyl diazoacetate with paraformaldehyde (CH_3OH, NaOH). Compound i rearranged quantitatively [catalytic $Rh(OAc)_2$, CH_2Cl_2, rt] to formylacetic ester ii thereby affording these water-soluble substances without resorting to a tedious extractive workup.

i $HOCH_2C(N_2)CO_2R$ $OHCCH_2CO_2R$ ii

(12) This perpendicular orientation of H_A to the Rh-C bond is based on an earlier proposal concerning free carbene rearrangements: A. Nickon, F. Huang, R. Weglein, K. Matsuo, H. Yagi, J. Amer. Chem. Soc., 96, 5263 (1974).

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