ORGANIC CHEMISTRY

SYNTHESIS AND CARBENE DECOMPOSITION OF FUNCTIONALLY-SUBSTITUTED DIAZOACETIC ESTERS.

4.* 2-AMINOETHYL DIAZOACETATES AND N-(2-HYDROXYETHYL)-N-ALKYLDIAZOACETAMIDES†

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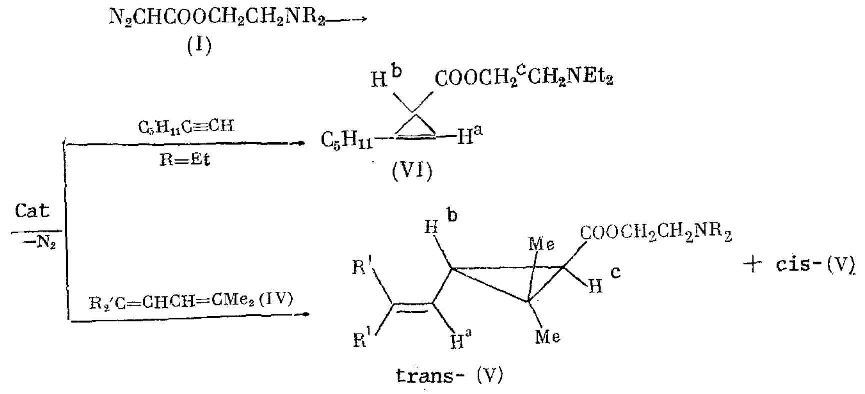
We have previously [1] described the synthesis of 2-N,N-dialkylamino)(I) and 2-(N-alkylamino)ethyl diazoacetates (II), and N-(2-hydroxyethyl)-N-alkyldiazoacetamides (III) from 2-bromoethyl diazoacetate and aliphatic amines. We have now examined the decomposition of (I)-(III) on treatment with 2 mole % of $Rh(OAc)_2$ or 2 mole % of an equimolar mixture of Cu and $CuSO_4$ in the presence of unsaturated compounds.

It has been found that the decomposition when carried out at 110°C in the presence of a mixture of Cu and $CuSO_4$ is probably of carbene type, and in the presence of a tenfold molar excess of dienes (IV) gives the corresponding cyclopropane adducts of aminoethoxycarbonylcarbenes, namely the 2-(N,N-dialkylamino)ethyl esters of trans and cis (55:45) vinylcyclopropanecarboxylic acids (V) in an overall yield of up to 40%. Cyclopropanation of (IV) (R' = Cl) in the presence of $Rh(OAc)_2$ at 60°C proceeds less efficiently as a result of gradual poisoning of the catalyst, to give (Vb) in 15% yield. In order to achieve full conversion of (I), it is necessary to add fresh catalyst during the course of the reaction. Denitration of (I) (R = Et) by treatment with $Rh(OAc)_2$ at 95-100°C in the presence of a 2.5-fold excess of 1-heptyne affords the hitherto unknown 2-(N,N-diethylamino)ethyl 2-pentylcyclopropene-3-carboxylate (VI) in 16% yield.



R = R' = Me (a), R = Et, R' = Cl (b), R = Et, R' = Me (c).

The presence of a nitrogen atom in (V) and (VI) simplifies considerably the purification of these compounds by conversion into the quaternary salts with acetic acid, these being readily freed from organic impurities.

The structures of (V) and (VI) were confirmed by their IR, PMR, and mass spectra (Table 1). The IR spectra of (V) showed absorption for (C–O) and (C=C), and that of (VI) showed characteristic absorption at 1803 cm^{-1} corresponding to vibrations of the cyclopropene double

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*For part 3, see [1].
†For a preliminary communication, see [2].

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TABLE 1. Properties of 2-Aminoethyl Vinylcyclopropanecarboxylates (V)

Compound	Yield, %	IR spectrum, ν, cm⁻¹		PMR spectrum (CCl_4, δ, ppm; J, Hz)					Mass spectrum, M⁺, m/z
				H^a					
		C=C	C=O	trans isomer	cis isomer	OCH_2	CH_2N	other protons	
(Va)	38	1640	1725	4,83 dm $^3J = 8$ $^4J < 2$	5,32 dm $^3J = 8$ $^4J < 2$	4,03 m	2,47 m	2,22 br.s [6H, $N(CH_3)_2$], 1,0–2,2 (Hb and Hc both isomers), 1.68 m (6H, CH_3), 1,23 s, 1,18 s 1,10 s (6H, CH_3- ring)	239
(Vb)	40 15 †	1650	1730	5,55 d $^3J = 8$	6,23 d $^3J = 8$	4,06 t $^3J = 6,5$	2,54 q $^3J = 6,5$	2,55 q [4H, $N(CH_2)_2$, $^3J = 7$], 2,20 d.d (H^b trans isomer, $^3J = 8$, $^4J = 5,5$), 1,67–2,10 (H^b and H^c cis isomers), 1.53 d (H^c trans isomer) 1.28 s, 1.27 s, 1.17 s (6H, CH_3- ring), 1,02 t (6H, CH_3, $^3J = 7$)	307, 309, 311
(Vc)	41	1635	1725	4,83 dm $^3J = 8$, $^4J < 2$	5,30 dm $^3J = 8$, $^4J < 2$	4,01 m	2,51 q $^3J = 7$	2,51 q [4H, $N(CH_2)_2$, $^3J = 7$], 0,87–2,01 (H^b and H^c, both isomers), 1,67 m (6H, CH_3, $^4J < 2$), 1,22 s, 1,20 s, 1,12 s (6H, CH_3- ring), 1,00 t (6H, CH_3, $^3J = 7$)	267

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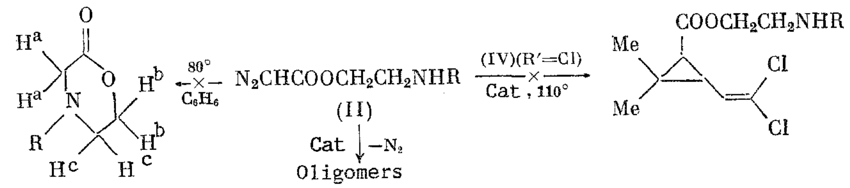
*2 mole % of an equimolar mixture of Cu and $CuSO_4$, 110°C, (IV):(I) = 10:1, molar.

†2 mole % $Rh(OAc)_2$, 60°C, (IV):(I) = 4:1, molar.

bond. Assignment of the signals for the trans and cis isomers in the spectra of (V) was carried out by comparison with the spectra of ethyl chrysanthemate and ethyl permethrinate [3]. The isomer ratio (55:45) was found from the integral intensities of the H^a protons. The mass spectra of (Va, c) and (VI) showed molecular ion peaks with m/z 239, 267, and 253 respectively, and the spectrum of (Vb) contained three molecular ion peaks with m/z 307, 309, and 311, due to the presence of the isotopes ^{35}Cl and ^{37}Cl.

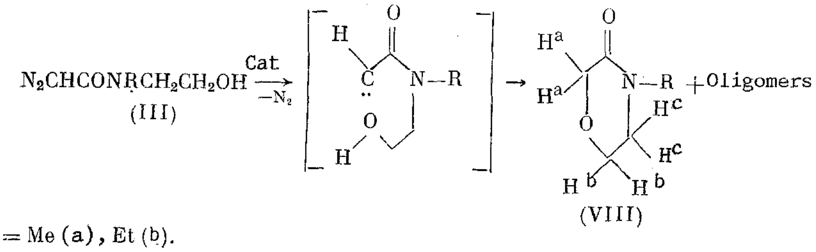
Hence, the 2-dialkylaminoethoxycarbonylcarbenes generated by the catalytic denitration of (I) are fairly reactive, so that they can be used for the synthesis of 2-dialkylaminoethyl cyclopropanecarboxylates, which are promising intermediates in fine organic syntheses [4].

In contrast to the dialkylamino compounds (I), the thermocatalytic decomposition of monoalkylated aminodiazoesters (II) by treatment with mixtures of Cu and $CuSO_4$ at 110°C in the presence of an excess of (IV) (R' = Cl) gives exclusively oligomeric compounds rather than the cyclopropane adducts, owing to the facile intermolecular insertion of the carbene center into the N–H bond. It is in fact known [5] that the thermocatalytic decomposition of ethyl diazoacetate by treatment with copper compounds in the presence of secondary aliphatic amines results in the quantitative insertion of the alkoxycarbonylcarbene at the N–H bond.



(VII)
R = Me (a), Et (b).

Ths reaction also predominates in the thermal denitration of (IIa) in benzene at 80°C to give, not the N-alkylmorpholin-2-ones (VII), as we reported earlier [6], but oligomeric products only. The error in [6] was due to the formation on reaction of 2-bromoethyl diazoacetate with $MeNH_2$ of the amide (IIIa) instead of the expected aminoester (IIa) [1], and such diazoamides are known to give the carbenes on thermocatalytic denitration, these readily undergoing cyclization [7, 8]. In fact, denitration of (III) by treatment with Cu and $CuSO_4$ at 80°C in benzene gave the N-alkylmorpholin-3-ones (VIII), the products of intramolecular insertion of the carbene carbon at the O–H bond (35-54%), in addition to oligomers.



R = Me (a), Et (b).

Intramolecular cyclization of the carbenes derived from (III) takes place efficiently even in the presence of unsaturated acceptors. For example, on treatment of (IIIa) with Cu and $CuSO_4$ at 110°C in the presence of a tenfold molar excess of (IV) (R' = Cl), the morpholinone (VIIIa) was obtained in 45% yield together with oligomeric products, whereas the corresponding cyclopropane derivatives were not found. The use of $Rh(OAc)_2$ as catalyst at 20-60°C resulted in reduced yields of (VIII) (15-20%), as a result of the rapid formation of oligomers.

The morpholinone (VIIIa) was obtained in the pure state by vacuum distillation, and (VIIIb) by column chromatography. The IR spectra of (VIII) showed absorption characteristic of stretching vibrations of the C=O group in cyclic amides [9] at 1660 cm^{-1}. In the PMR spectra, the chemical shifts of protons H^a (3.94 ppm) and H^b (3.80 ppm), H^c (3.20 ppm), and CH_3 (2.86 ppm) in (VIIIa) are in good agreement with the values reported in [10, 11], and differ considerably from those of the analogous protons in (VIIa) (2.80, 4.05, 2.30, and 2.00 ppm respectively) [12]. The mass spectra of (VIII) show peaks for the molecular ions.

Hence, intramolecular cyclization of (III) provides a convenient method for the synthesis of N-alkylmorpholin-3-ones, which are particularly useful as selective extractants for aromatic hydrocarbons [13].

EXPERIMENTAL

The conditions for the recording of IR, PMR, and mass spectra have been reported previously [1].

The starting 2,5-dimethylhexa-2,4-diene (IV, R' = Me) was obtained as described in [14], and 1,1-dichloro-4-methylpenta-1,3-diene (IV, R' = Cl) as in [15]. The syntheses of 2-(N,N-dialkylamino)ethyl diazoacetates (I), 2-(N-alkylamino)ethyl diazoacetates (II), and N-(1-hydroxyethyl)-N-alkyldiazoacetamides (III) have been described in [1].

2-(N,N-Dialkylamino)ethyl Vinylcyclopropanecarboxylates (V). To a suspension of 0.0032 g (0.05 mmole) of copper powder and 0.008 g (0.05 mmole) of anhydrous $CuSO_4$ in 2.0 g of (IVa) (R' = Me) was added at 110°C over 3 h a solution of 1.0 g (5.4 mmoles) of (Ib) in 3.94 g of (IVa) (total amount of (IV) 59.4 mmoles). The mixture was stirred for 30 min until evolution of nitrogen ceased, and diluted with 5 ml of CCl_4 and 5 ml of water. The aqueous layer was acidified with 5% aqueous acetic acid to pH 4-5. The organic layer was separated, the aqueous layer extracted with CCl_4 (2 × 5 ml), neutralized with 5% ammonia to pH 8, and again extracted with 5 ml of CCl_4. The latter extract was dried over anhydrous $MgSO_4$ and evaporated to give 0.55 g (41%) of a mixture of 2-(N,N'-diethylamino)ethyl trans- and cis-chrysanthemates (55:45) (Vc) (Table 1).

Obtained similarly were the 2-(N,N-dimethylamino)ethyl trans- and cis-chrysanthemates (Va) and the 2-(N,N-diethylamino)ethyl trans- and cis-permethrinates (Vb) (Table 1).

2-(N,N-Diethylamino)ethyl 1-Pentacyclopropene-3-carboxylate (VI). To a solution of 0.12 g (0.5 mmole) of $Rh(OAc)_2$ in 1.0 g of 1-heptyne was added over 3 h at 95°C a mixture of 1.8 g (10 mmoles) of (Ib) and 1.4 g of 1-heptyne (total amount of 1-heptyne, 25 mmoles). The mixture was stirred for 2 h, until evolution of nitrogen ceased, then cooled to 20°C and diluted with 5 ml of CCl_4. The resulting solution was filtered through a thin layer (0.5-1.0 cm) of silica gel, and the filtrate diluted with 5 ml of water. The aqueous layer was separated and treated with HCl and ammonia, as described above, to give 0.42 g (16.6%) of (VI), n_D^{20} 1.4731. IR spectrum (ν, cm^{-1}): 1730 (C=O), 1803 (C=C). PMR spectrum (in CCl_4, δ, ppm): 6.22 m (H^a), 4.00 m ($2H^b$), 2.00 d(H^a, J_{ba} = 1.2 Hz), 2.2-2.7 (8H), 0.7-1.8 (15H). Mass spectrum: M^+, m/z 253.

N-Alkylmorpholin-3-ones (VIII). To a suspension of 50 μmoles of copper powder and 50 μmoles of anhydrous $CuSO_4$ in 10 ml of benzene was added at 80°C over 2 h a solution of 0.65 g (4.5 mmoles) of (IIIa) in 85 ml of benzene. The mixture was stirred for a further 30 min, until evolution of nitrogen had ceased completely, and filtered. The filtrate was evaporated, and the residue distilled under reduced pressure to give 0.28 g (54%) of N-methylmorpholin-3-one (VIIIa), bp 60°C (2.5 mm), n_D^{20} 1.4753. IR spectrum (ν, cm^{-1}): 1660 (C=O). PMR spectrum (in CCl_4, δ, ppm): 3.94 s ($2H^a$), 3.80 m ($2H^b$), 3.20 m ($2H^c$), 2.86 s (CH_3). Mass spectrum: M^+, m/z 115.

Similarly obtained, and purified by column chromatography on silica gel (eluent benzene, followed by ether) was N-ethylmorpholinone (VIIIb), yield 35%, n_D^{20} 1.4731. IR spectrum (ν, cm^{-1}): 1660 (C=O). PMR spectrum (CCl_4, δ, ppm): 3.96 s ($2H^a$), 3.84 m ($2H^b$), 3.93 q (CH_2Me, ^3J = 7 Hz), 3.33 m ($2H^c$), 1.14 t (CH_3). Mass spectrum: M^+, m/z 129.

CONCLUSIONS

1. Thermocatalytic decomposition of 2-(dialkylamino)ethyl diazoacetates with 2 mole % of an equimolar mixture of Cu and $CuSO_4$ at 110°C, or with 2 mole % of $Rh(OAc)_2$ at 60-100°C, is of the carbene type, and in the presence of dienes and acetylenes affords respectively the cyclopropane- and cyclopropenecarboxylate esters.

2. Facile intramolecular cyclization has been observed in N-(2-hydroxyethyl)-N-alkyldiazoacetamides to give N-alkylmorpholin-3-ones on treatment with Cu and $CuSO_4$ at 80-110°C.

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