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LETTERS

Photolysis of Dipropyldiazirine and Trapping of Dipropylcarbene With Piperidine.

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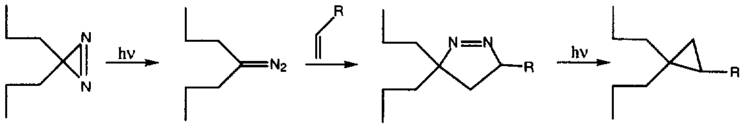
Abstract: Photolysis (350 nm) of dipropyldiazirine in methylene chloride at 4°C produces a mixture of E and Z 3-heptene in 81% yield in an *E/Z* ratio of 1.8. Tetrapropylazine was formed in less than 5% yield. Photolysis of dipropyldiazirine in the presence of piperidine leads to the formation of a carbene-amine adduct. In the presence of 0.06 M piperidine the yield of adduct is 48%, the yield of *E* and Z 3-heptene is 47% and the *E/Z* ratio of 3-heptenes is 1.1. The results show that heptene is formed by three pathways. One pathway involves dipropylcarbene formed directly from the diazirine, the other pathways are attributed to ionic and photochemical reactions of 4-diazoheptane and to the excited state of the diazirine precursor. Dipropylcarbene can be easily intercepted with a simple trap. The yield of this process is limited by the efficiency with which the precursor forms the carbene. © 1999 Elsevier Science Ltd. All rights reserved.

Reports of efficient bimolecular reactions of *simple* alkyl and dialkyl carbenes are scarce.[1] This has been attributed to a prohibitively rapid rate of competing 1,2 hydrogen migration reactions which form alkenes. However, recent flash photolysis experiments indicate that simple dialkylcarbenes have lifetimes that are sufficiently long to allow their efficient capture with suitable traps.[2] This conclusion is reinforced by high level molecular orbital calculations which predict that the 1,2 rearrangements of dialkylcarbenes must overcome barriers in excess of 5 kcal/mol.[3]

These conclusions have prompted this investigation of the photolysis of dipropyldiazirine **1**[4] in the presence of piperidine. Piperidine was used as trap instead of an alkene, which we feared might react with putative diazo intermediate **2** to ultimately give the same product as a carbene cycloaddition reaction, and complicate the interpretation of the mixture of products obtained.



1 2

Photolysis (350 nm, Ray-o-net reactor, 4°C , 5 hours) of **1** in $CDCl_3$(^{1}H-NMR) or CH_2Cl_2(GC analysis) produces E and Z 3-heptene (**3** *E,Z*) in 81% yield (^{1}H-NMR-benzene internal standard). Tetrapropylazine was formed in very low yield (≤5%).[5]

Upon photolysis of **1** in the presence of 0.1 M acrylonitrile in CH_2Cl_2 the yield *E, Z* 3-heptene fell to 48%. This implies that diazirine **1** isomerizes to diazo compound **2**, upon photolysis, in 33% yield, assuming that the

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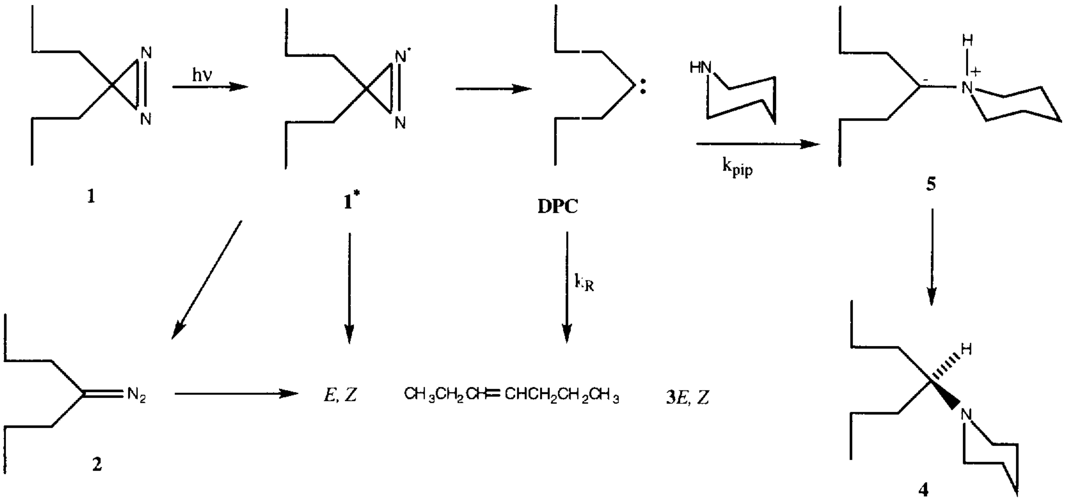
reduction in yield of **3** *E, Z* is entirely due to scavenging the diazo compound before it suffers further photolysis or ionic decomposition to form **3**.[6]

In fact, upon partial photolysis of **1** (30 minutes, 4°C) the CH_2Cl_2 solution turned pink ($\lambda_{max} \approx 500$ nm). The pink color is attributed to **2** which had a half life of approximately one hour in the dark at ambient temperature. The pink color was discharged immediately upon addition of 0.1 M acrylonitrile but was not influenced by the addition of piperidine, indicating that the diazo compound reacts slowly, if at all, with the amine.

Adduct **4** is produced upon photolysis of **1** in CH_2Cl_2 containing piperidine,[5] presumably by capture of dipropylcarbene (DPC) to form an ylide **5** which subsequently rearranges.



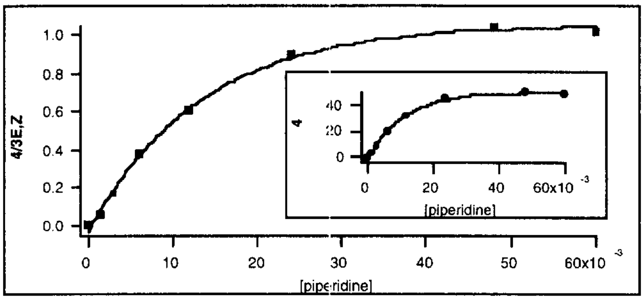
No adduct is formed if piperidine is added to the sample following photolysis, further proof that **4** is not formed from diazo compound **2**. Addition of acryonitrile (0.1M) to the samples post photolysis had no effect on the yield of **3***E,Z* and **4**.

The yields of **3** *E,Z* and **4** are dependent on the concentration of piperidine (Table 1, Figure 1). The yield of **4** reaches a maximum and the yield of **3** *E,Z* its minimum when [piperidine] ≈ 0.05 M. Piperidine does not completely quench the yield of **3** *E,Z* demonstrating that the 3-heptenes are formed by more than one mechanism.[7,8] This is further illustrated by the change in the **3***E*/**3***Z* ratio with piperidine concentration.[8]

Table 1. Products formed upon photolysis (350 nm) of 1 in CH_2Cl_2 at 4°C (± 2%)

[piperidine]	3*E,Z*	3E/3Z	4
0	81	1.77	0
0.0015	65	1.69	3.5
0.0030	55	1.36	9.4
0.0060	53	1.27	20
0.012	51	1.19	31
0.024	50	1.14	45
0.048	47	1.10	49
0.060	47	1.08	48

Figure 1. The ratio of adduct **4** / alkenes **3***E,Z* produced upon photolysis of **1** (CH_2Cl_2, 350nm 4°C) as a function of [piperidine] (±2%,GC)



Thus, we conclude that only 42% of the *total* yield of **3** E,Z is derived from DPC formed directly from diazirine **1**. The acrylonitrile quenching experiment indicates that 33% of the total heptenes formed derive from diazo compound **2**, meaning ~ 25% of the total heptene yield derives from a third mechanism, perhaps a rearrangement in the excited state of the diazirine precursor (1^*).

In summary, our results show that a simple dialkylcarbene can be easily intercepted with a trap to form an adduct, as predicted by recent kinetic[2] and theoretical work.[3] The main limitation to the trapping reaction is the efficiency with which the precursor generates the carbene. This study implies that dialkylcarbenes may have synthetically useful bimolecular chemistry when highly efficient precursors become generally available.

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4. The concentration of diazirine (**1**) in $CDCl_3$ was obtained by ^{1}H-NMR integration with benzene as a standard. The absorption coefficient (ε) of the diazirine was 175 at 350 nm (CH_2Cl_2). Product analyses were performed using an HP-6890 Series GC System with an HP-1 methyl siloxane capillary column (40.0m x 100 µm x 0.20 µm). The gas chromatograph was linked to an HP 5973 Mass Selective Detector. Yields were quantified with

an external standard (decane). The retention times of *E,Z*-3-heptene (**3** *E,Z*), decane and adduct (**4**) were 5.84, 5.90, 10.69 and 14.09 min. The response factors with decane of *E,Z*-3-heptene (**3** *E,Z*) and adduct (**4**) were 0.95, 0.92 and 0.79, respectively, Diazirine **1** was prepared by condensing 30 mL of ammonia into 10 mL of dry methanol at -35^0. To this was added 10 mL solution of *tert*-butylhypochloride (Mintz, M.J.; Walling, C., Organic Synthesis, Vol. 5, p. 184). 4-heptanone was added dropwise and stirred 4h at -40^0. The solution was allowed to warm to RT. Water was added to the reaction which was extracted with dichloromethane. The combined dichloromethane extract was dried and concentrated to yield the expected diazirine which was oxidized with chromium trioxide using the procedure of Bayley and Knowles (Bayley, H., Knowles, J.R. *Biochemistry*, **1980**, *19*, 3884). ^{1}H-NMR(200MHz, $CDCl_3$ ppm) 1.35(m,4H), 1.12(m, 4H), 0.85(m, 6H) ^{13}C-NMR(63MHz, $CDCl_3$, ppm) 35.0, 28.6, 17.0, 13.8 UV(pentane) 351nm MS(EI) m/e (rel.intensity) 98(M-28, 33), 69(54), 56(58), 41(100).

5. Mixtures of products formed on photolysis were analyzed by capillary GC or by ^{1}H-NMR. *E,Z*-3 heptenes were identified with commercially available authentic samples. Azine was prepared from 4-heptanone and hydrazine ^{1}H-NMR (200MHz, $CDCl_3$, ppm) 2.20 (tt, 8H, J=10Hz), 1.59 (m, 4H) 1.39 (m, 4H) 0.89 (tt, 12H, J=10Hz); ^{13}CNMR (63MHz, $CDCl_3$, ppm) 164.8, 38.6, 32.7, 19.8, 19.4, 14.4, 14.0. MS (EI m/e (rel. intensity) 224(4), 181 (100), 140 (92), 112 (55), 70 (86). Adduct **4** (Barney, C.L.; Huber, E.W.; McCarthy, J.R., *Tetrahedron Letters*, *31* No. 39, 5547-5550) was prepared by sodium cyanoborohydride reduction of the enamine of 4-heptanone and piperidine ^{1}H-NMR (200MHz, $CDCl_3$, ppm) 2.4(t, 4H), 2.25(t, 1H), 1.1-1.6(m, 14H), 0.85(t, 6H); ^{13}C-NMR (63MHz, $CDCl_3$, ppm) 84.0, 69.1, 52.1, 47.0, 45.1, 40.0, 34.0.; MS(EI) m/e (rel.intensity) 183(M, 1), 140(100), 98(3), 84(3), 55(3), 41(4); HRMS(EI) calcd for $C_{12}H_{25}N_1$ 183.1988 found 183.1981

6. The diazo compound may form dipropylcarbene (and then heptene) under our experimental conditions or form heptenes by ionic processes.

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