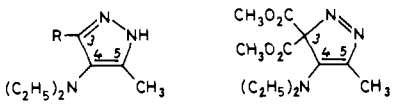
Communications to the Editor

Diazocarbonyl Compounds and 1-Diethylaminopropyne

Sir:

1,3-Dipolar cycloadditions of diazomethane are HO (diazomethane)-LU (dipolarophile) controlled;[1] enamines and ynamines with their high LU energies do not react. Introduction of carbonyl functions into diazomethane lowers the orbital energies to such an extent that the diazoacetic ester and diazomalonic ester are type II 1,3 dipoles in Sustmann's classification,[2,3] and concerted cycloadditions to enamines[4] and ynamines become feasible through HO (dipolarophile)-LU (diazoalkane) interaction. The only reported addition to an ynamine is that of diazofluorene and 1-diethylaminopropyne affording a spiro adduct (6 h, 80 °C, 22%) of which the addition direction was not clarified.[5]

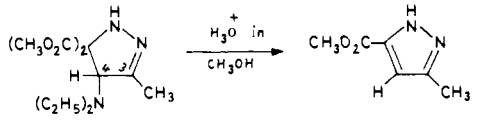


1 R = CO_2CH_3
2 R = H

3

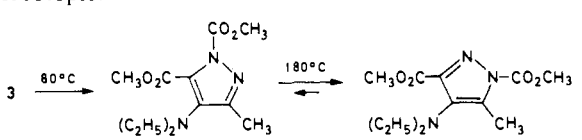
Methyl diazoacetate and 1-diethylaminopropyne furnished in refluxing hexane (6 h) the oily aminopyrazole **1** in 89% yield:[6] bp 140–150 °C (0.3 mm); NMR δ 2.25 (s, 5-CH_3), 3.85 (s, OCH_3), 12.4 (br, NH). Alkaline hydrolysis and decarboxylation (310 °C) produced 4-diethylamino-5-methylpyrazole (**2**). The sharp NMR singlets for 5-CH_3 (δ 2.21) and 3-H (7.35), i.e., the absence of allyl coupling, would not be consistent with the product of the opposite addition direction (J = 0.5 Hz for the isomeric 3-diethylamino-5-methylpyrazole). Further evidence comes from the linking with the diazomalonic ester adduct.

Dimethyl diazomalonate reacted with the ynamine in ether at 0 °C to give 66% bright yellow needles of the 3*H*-pyrazole **3**: mp 77–78 °C; NMR δ 1.15, 3.40 (t and q, J = 7.0 Hz, 2 NCH_2CH_3), 2.48 (s, 5-CH_3), 3.79 (s, 2 OCH_3). Aromatization makes one ester group of **3** subject to nucleophilic removal. In cold methanol (4 weeks), faster in diethylamine, **3** is quantitatively converted to **1**.



4 5

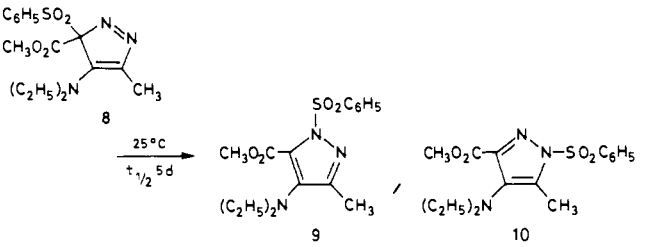
Reduction of the azo bond in **3** with sodium borohydride in methanol at 0 °C yielded via the ene-hydrazine the cyclic hydrazone **4** (95%). The NMR singlets for 3-CH_3 (δ 1.97) and 4-H (4.97) established the original addition direction as did the methanolysis which rendered 74% methyl 3-methylpyrazole-5-carboxylate (**5**), identical with the product from diazoethane and methyl propiolate. The ester groups of **4** are nonequivalent (δ 3.32, 3.43) and the NCH_2 protons are diastereotopic.



6 7

The thermal van Alphen-Hüttel rearrangement[7,8] of the 3*H*-pyrazole **3** to the aromatic 1,5-dicarboxylic ester **6** was complete after 15 h refluxing in hexane; $t_{1/2}$ = 30 days at 25 °C. The high IR frequency of 1756 cm^{-1} and the high δ 4.02 are typical for NCO_2CH_3. Under the conditions of distillation, 180 °C (12 mm), **6** underwent a further 1,5-sigmatropic shift, until a 1:3 equilibrium of **6** and **7** was established: mp (**7**) 46–48 °C; NMR δ 3.90, 4.05 (2 s, 2 OCH_3). The singlet of 3-CH_3 in **6** (δ 2.23) is deshielded in **7** by the vic. ester group and shows up at δ 2.48. Diethylamine converts both **6** and **7** to the diazoacetic ester adduct **1** and methyl *N,N*-diethylcarbamate.

The fast cycloaddition of methyl diazo(phenylsulfonyl)-acetate in ether at 0 °C afforded quantitatively the oily 3*H*-pyrazole **8** which shows a low-field NCH_2 at δ 4.04 (δ 3.40 in **3**). A phenylsulfonyl shift occurred at room temperature and produced **9** and **10** in a 7:2 ratio. Methanolic sodium hydroxide (not diethylamine) produced 83% **1** from **9** and **10**.

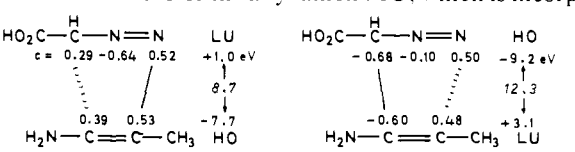


8 9 10

The addition of methyl diazoacetate to methyl propiolate—not described before—yielded 88% dimethyl pyrazole-3,5-dicarboxylate (3 days, 25 °C). This addition direction is opposite that which diazocarbonyl compounds display toward enamines[4] and ynamines which invariably furnish 4-amino-substituted pyrazolines or pyrazoles. The *bidirectionality* of these 1,3 dipoles is incompatible with diradical intermediates. It is not mandatory that ethylenes and acetylenes with electron-attracting substituents accept the 1,3 dipole in one direction, whereas those with electron-releasing substituents use the other addition direction. PMO theory[3,9,10] and experiment reveal that the switching of the orientation can occur at every place on the scale of electron density of the ethylenic or acetylenic bond, dependent on the nature of the 1,3 dipole.

Ethoxyacetylene does not react with diazoacetic ester, but combines with diazomethane to give 4-ethoxypyrazole, whereas ethylthioacetylene gives rise to 3-ethylthiopyrazole.[11] 3-Alkylpyrazoles result from diazomethane and 1-alkynes.[12] Thus, diazoalkanes appear to display the orientational switching between acetylenic thioethers and ethers.

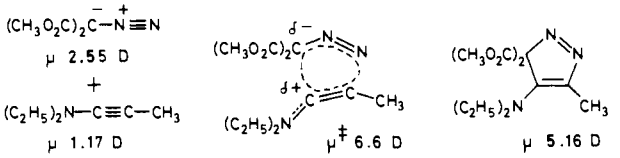
The diagrams below offer the CNDO/2 calculated[13] atomic orbital coefficients c of the allyl anion MO, which is incorporated in the 1,3 dipole, and those of the ynamine. The orbital energies were estimated on the basis of ionization potentials, $\pi \rightarrow \pi^*$ transitions and electron affinities.[14] Both frontier orbital interactions favor the same orientation, the one experimentally observed, although the first interaction is dominant owing to the smaller energetic separation.



Are we dealing with a one-step cycloaddition or with the

0002-7863/79/1501-3647$01.00/0

reaction via a zwitterionic intermediate? We measured the dependence of the rate constant on solvent polarity, based on the IR diazo absorption at 2129 cm^{-1}, for diethylaminopropyne + dimethyldiazomalonate and observed a small positive effect ($10^5 k_2$ (L mol^{-1} s^{-1}) at 80.3 °C): decalin, 42; toluene, 45; dioxane, 41; chlorobenzene, 69; HMPTA, 132; DMF, 158; Me_2SO, 265. When log k_2 was plotted vs. the empirical polarity parameter E_T,[15] a linear function ($r = 0.95$) resulted.



Whereas the data rule out a zwitterionic intermediate, the question of transition-state polarity still deserves attention. We determined the dipole moments of reactants and adduct (benzene, 25 °C). The log k_2 values above fit fairly well a linear relation with $(\epsilon - 1)/(2\epsilon + 1)$ with ϵ being the dielectric constant of the solvent. Based on the Kirkwood-Laidler-Eyring equation,[16] we calculated from the slope of the line and from the dipole moments and molecular volumes of the reactants the dipole moment of the transition state, $\mu = 6.6$ D.[17] Unequal bond formation in the transition state of the concerted cycloaddition induces, in accordance with the PMO treatment, a partial charge separation which exceeds that of the cycloadduct slightly.

References and Notes

(1) Geittner, J.; Huisgen, R.; Sustmann, R. *Tetrahedron Lett.* **1977,** 881–884.
(2) Sustmann, R. *Tetrahedron Lett.* **1971,** 2717–2720. *Pure Appl. Chem.* **1974,** *40,* 569–593.
(3) Huisgen, R. *J. Org. Chem.* **1976,** *41,* 403–419.
(4) Huisgen, R.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1979,** *18,* in press.
(5) Dürr, H.; Schmidt, W. *Justus Liebigs Ann. Chem.* **1974,** 1140–1149.
(6) Satisfactory CH and N analyses were obtained for all new compounds.
(7) van Alphen, J. *Recl. Trav. Chim. Pays-Bas* **1943,** *62,* 485–490, 491–496.
(8) Hüttel, R.; Riedl, J.; Martin, H.; Franke, K. *Chem. Ber.* **1960,** *93,* 1425–1432. Hüttel, R.; Franke, K.; Martin, H.; Riedl, J. *ibid.* **1960,** *93,* 1433–1446.
(9) Houk, K. N. *J. Am. Chem. Soc.* **1972,** *94,* 8953–8955. Houk, K. N.; Sims, J.; Watts, C. R.; Luskus, L. J. *ibid.* **1973,** *94,* 7301–7315.
(10) Bastide, J.; El Ghandour, N.; Henri-Rousseau, O. *Tetrahedron Lett.* **1972,** 4225–4228; *Bull. Soc. Chim. Fr.* **1973,** 2290–2293.
(11) Groen, S. H.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1961,** *80,* 879–884.
(12) Review: Bastide, J.; Hamelin, J.; Texier, F.; VoQuang, Y. *Bull. Soc. Chim. Fr.* **1973,** 2567–2574.
(13) We express our gratitude to Professor R. Sustmann, Essen.
(14) Reissig, H.-U. Ph.D. Thesis, University of Munich, 1978, pp 131–133.
(15) Dimroth, K.; Reichardt, C.; Siepmann, T.; Bohlmann, F. *Justus Liebigs Ann. Chem.* **1963,** *661,* 1; Reichardt, C. "Lösungsmittel-effekte in der organischen Chemie", Verlag Chemie: Weinheim-Bergstr., Germany, 1969.
(16) Kirkwood, J. G. *J. Chem. Phys.* **1934,** *2,* 351. Glasstone, S.; Laidler, K. J.; Eyring, H. "The Theory of Rate Processes", McGraw Hill: New York, 1941; p 419.
(17) For details of the treatment, cf. Steiner, G.; Huisgen, R. *J. Am. Chem. Soc.* **1973,** *95,* 5056.

Rolf Huisgen,* Hans-Ulrich Reissig, Helmut Huber

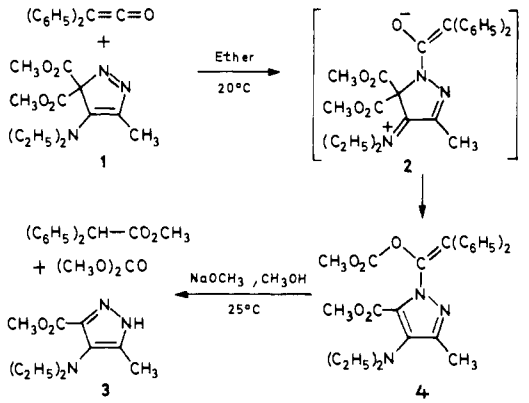
Institut für Organische Chemie der Universität München Karlstr. 23, 8000 München 2, West Germany

Received February 24, 1979

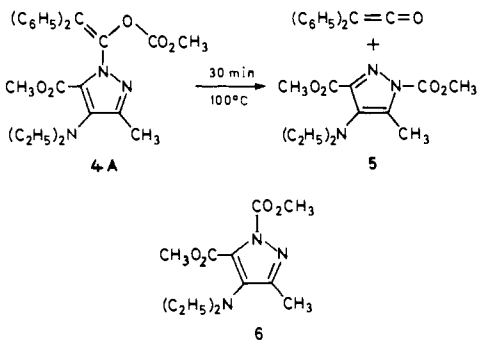
Conducted Tour Mechanism of Ester Group Migration in a 3*H*-Pyrazole

Sir:

Dimethyl 4-dimethylamino-5-methyl-3*H*-pyrazole-3,3-dicarboxylate (**1**)[1] and diphenylketene in ether at 25 °C produced quantitatively the colorless crystals of a 1:1 adduct, mp 72–73 °C.[2] The ^{13}C chemical shifts indicate that all five skeletal carbon atoms are sp^2 hybridized which is incompatible with a cycloadduct. The ketene *O,N*-acetal structure **4** was suggested by the base-catalyzed methanolysis which provided 97% pyrazole **3**[1] besides methyl diphenylacetate and dimethyl carbonate. The similarity of the NMR spectra of **3** and **4** allude to an aromatic pyrazole ring in **4**. The IR absorption at 1777 cm^{-1} is assigned to the enol ester carbonyl and the weak band at 1659 cm^{-1} to the CC double bond.

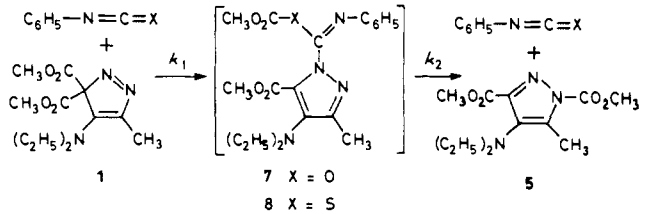


The diethylamino group confers nucleophilicity on the heterodiene system of **1**. In a likely mechanism, diphenylketene attacks at N-1 and affords the iminium enolate zwitterion **2**. Now the anionic oxygen takes over an ester group from the quaternary carbon atom, a process which is facilitated by the aromatization of the heterocycle.



At 100–110 °C **4** was smoothly cleaved, whereby diphenylketene was distilled under high vacuum and furnished 98% methyl diphenylacetate with methanol. The residue turned out to be pure 1,3-dicarboxylic ester **5** which is formed irreversibly; **5** is inert to diphenylketene. The thermal aromatization of the 3*H*-pyrazole **1** by a twofold 1,5-sigmatropic shift, **1** → **6** ⇌ **5**, was described in the preceding communication; the second step requires ~180 °C and results in a 1:3 equilibrium of **6** and **5**.[1] Thus, **1** cannot be an intermediate in the conversion of **4** to **5** + diphenylketene.

The ketene acylal group in **4** is an acylating reagent. In the return of the ester group to C-5, i.e., the regeneration of **1**, the pyrazole aromaticity would be sacrificed. However, the transfer of the ester group to N-2, starting from the rotamer **4A**, offers an attractive pathway. Had we carried out the reaction of **1** with diphenylketene at 100 °C, a mere isomerization, **1** → **4**, would have been observed.



0002-7863/79/1501-3648$01.00/0