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ON SOME AZOMETHINE IMINES (+)

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The reaction between diphenyldiazomethane and azocarbonyl compounds having trans configuration furnishes the corresponding 3,4-dihydro-1,3,4-oxadiazoles $^{1)}$. The condensation with ethyl azodicarboxylate and with 4-phenyl-1,2,4-triazolin-3,5-dione gives on the contrary unstable products: we wish now to report additional evidence for the proposed structures I resp. VI of azomethine imines. Hydrolysis, alcoholysis and IR spectra have already been discussed $^{1)}$.

In analogy to the behaviour of azomethine imines prepared from diazoalkanes and aromatic diazocyanides $^{2)}$, I and VI undergo 1,3-cycloaddition with acetylenedicarboxylate, maleate and phenylisocyanate, giving rise to the reactions outlined in Chart 1.

A mixture of 12.6 g. of azomethine imine I, prepared as already described $^{1)}$, and 7.9 g. of dimethyl acetylenedicarboxylate was left at room temperature for 3 days. The semisolid product was ground with light petroleum and recrystallized from ethanol, giving 12.95 g. (73 % yield) of 1,2-dicarbethoxy-3,3-diphenyl-4,5-dicarbomethoxy-2,3-dihydropyrazole (II) as colourless crystals, m.p. 131-132° (Anal. Calcd. for $C_{25}H_{26}N_2O_8$: C, 62.23; H, 5.43; N, 5.81. Found: C, 61.94; H, 5.43; N, 5.88).

Hydrolysis of pyrazole II with boiling methanolic KOH gave a crude potassium salt, whose aqueous solution was percolated through a Castel C 300 column. Evaporation of the solution leaved a 73 % yield of 5-pyrazolone-3-carboxylic acid, identified through comparison with an authentic sample $^{3)}$. From the methanolic mother liquid a 82 % yield of

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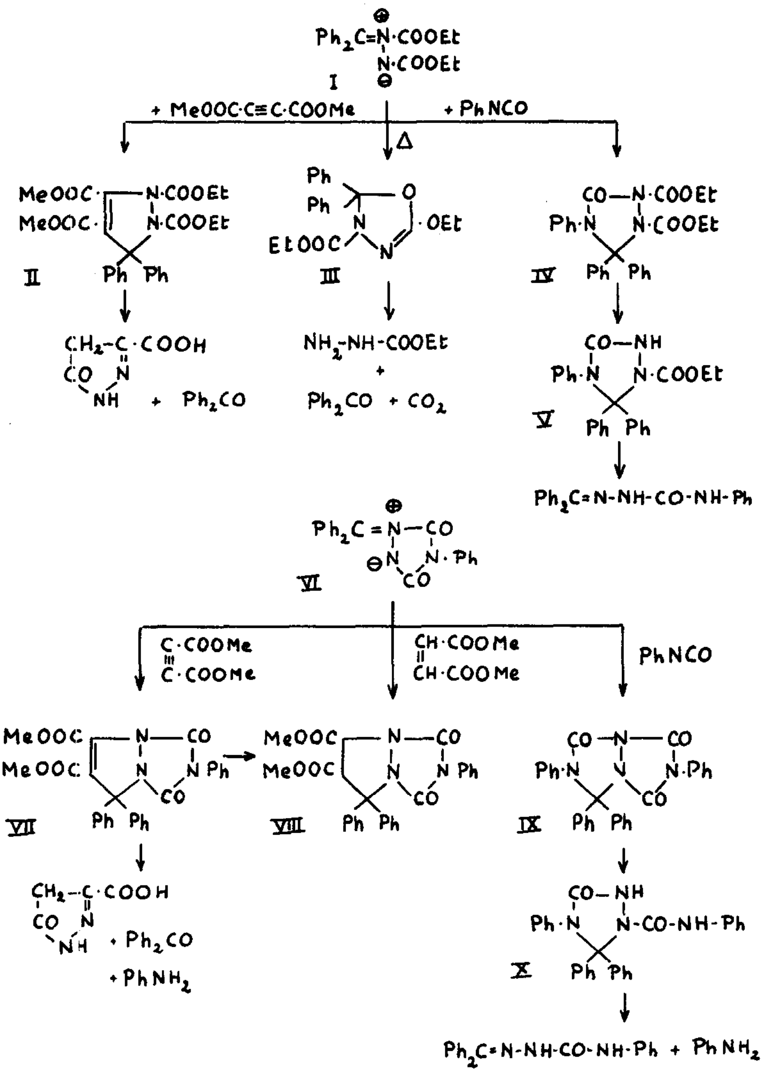
(+) Reactions of diaryldiazoalkanes. Part V.

Chart 1


I
+ MeOOC·C≡C·COOMe
Δ
+ PhNCO
II
III
IV
V
Ph₂C=N-NH-CO-NH-Ph
VI
C·COOMe ≡ C·COOMe
CH·COOMe = CH·COOMe
PhNCO
VII
VIII
IX
X
+ Ph₂CO
+ PhNH₂
NH₂-NH-COOEt + Ph₂CO + CO₂
Ph₂C=N-NH-CO-NH-Ph + PhNH₂

benzophenone was recovered.

Azomethine imine I did not react with dimethyl maleate, since ring closure was more rapid than 1,3-cycloaddition.

A solution of 10.2 g. of I in 25 ml. of dry carbon tetrachloride was heated at 40° for 20 days. After removal of the solvent the waxy residue, washed with a mixture of light petroleum and diethyl ether (4:1) and recrystallized from 90 % ethanol, gave 5.94 g. (58 % yield) of 2-ethoxy-4-carbethoxy-5,5-diphenyl-4,5-dihydro-1,3,4-oxadiazole (III) as colourless prisms, m.p. 82-83° (*Anal.* Calcd. for $C_{19}H_{20}N_2O_4$: C, 67.04; H, 5.92; N, 8.23; found: C, 66.93; H, 5.99; N, 8.27).

Structure of oxadiazole III is based on IR evidence and has been confirmed by acid hydrolysis and decarboxylation to benzophenone (99 % yield) and ethyl hydrazinecarboxylate, isolated as benzalderivative (71 % yield), m.p. 135-136°, identified through IR spectrum, m.p. and mixed m.p. with an authentic sample4). Cf. behaviour of I toward hydrolysis1).

At room temperature the isomerization of I to III proceeds more slowly; for instance, after 30 days at 17° the yield of III has been the same as after 24 hrs. at 40° (IR spectra comparison).

To a solution of 12.4 g. of azomethine imine I in 20 ml. of dry CCl_4 4.0 ml. of phenylisocyanate were added. The mixture, left aside for 3 days, slowly crystallized. After removal of the solvent *in vacuo*, the residue, recrystallized from ethanol, gave 14.4 g. of diethyl 3,3,4-triphenyl-1,2,4-triazolid-5-one-1,2-dicarboxylate (IV), m.p. 147-148° (86 % yield)(*Anal.* Calcd. for $C_{26}H_{25}N_3O_5$: C, 67.96; H, 5.48; N, 9.15. Found: C, 68.16; H, 5.57; N, 9.35).

Hydrolysis of IV with boiling ethanolic KOH gave after 5 hrs. a crude potassium salt, which was dissolved in cold water and acidified with acetic acid to give a 91 % yield of ethyl 3,3,4-triazolid-5-one-2-carboxylate (V), m.p. 178° from ethanol (*Anal.* Calcd. for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.10; H, 5.49; N, 10.90). The latter product was very resistent to further hydrolysis, but a 32 hrs. boiling with ethan. KOH allowed to isolate, besides 70 % unchanged product, a small quantity (5 % yield) of benzophenone phenylsemicarbazone, m.p. 163°, identified by IR spectrum and mixed m.p.5) This result confirms structure IV and rules but isomeric structures.

A mixture of 10.23 g. of azomethine imine VI[1] and 20 ml. of dimethyl acetylenedicarboxylate was cautiously heated with stirring up to 40°. When the exothermic reaction had subsided, stirring was suspended and the mixture left aside for 24 hrs. Removal of the solvent and recrystallization from ethanol gave 10.4 g. (72 % yield) of pyrazolo-triazolone VII as colourless needles, m.p. 178-178.5° (Anal. Calcd. for $C_{27}H_{21}N_3O_6$: C, 67.07; H, 4.38; N, 8.70. Found: C, 67.01; H, 4.55; N, 8.88).

Catalytic hydrogenation of VII with 10 % Pd/C in ethanolic solution at room temperature and pressure consumed one mole of hydrogen. The undissolved material was extracted twice with hot acetic acid and the combined extracts cooled. The separated white crystals were filtered off and recrystallized from acetic acid to give a 60 % yield of product VIII, m.p. 223-224° (Anal. Calcd. for $C_{27}H_{23}N_3O_6$: C, 66.79; H, 4.78; N, 8.66. Found: C, 66.28; H, 4.90; N, 8.59).

The same product VIII was obtained by condensation at 40° of azomethin imine VI with dimethyl maleate: after 10 days heating the yield was 60 %.

Structure VII was supported by the results of hydrolytic cleavage with boiling ethanolic KOH. Operating as above reported with II, a 42 % yield of an acidic product was obtained, along with benzophenone (54 % yield), aniline (isolated as hydrochloride, 67 % yield) and a small quantity (8 % yield) of an acid, no further investigated, for whose methylester, dec.p. 194-195°, analytical data suggest a formula $C_{26}H_{23}N_3O_5$. The above mentioned acidic product was identical, according to its IR spectrum, m.p. and mixed m.p., with an authentic sample of 5-pyrazolone-3-carboxylic acid[3].

A mixture of 3.41 g. of azomethine imine VI and 6.0 ml. of phenylisocyanate was kept at 32° for 24 hrs. Excess of phenylisocyanate was stripped off in vacuo, the residue was washed with hot ethanol and recrystallized from acetic acid to give 3.88 g. (76 % yield) of triazo-triazolone IX, m.p. 218-219° (Anal. Calcd. for $C_{28}H_{20}N_4O_3$: C, 73.03; H, 4.38; N, 12.17. Found: C, 73.05; H, 4.11; N, 12.31). The same product was also obtained by simple boiling of the solution of azomethine imine VI in CCl_4: after 12 hrs. the yield was 57 %.

Hydrolytic cleavage of IX was carried out with boiling ethanolic KOH: after 5 hrs. the mixture was evaporated and worked up as before. Besides aniline hydrochloride (28 % yield) and benzophenone phenylsemicarbazone (28 % yield), an acidic product was obtained in 35 % yield; colourless needles (from ethanol), m.p. 158-159° (Anal. Calcd. for $C_{27}H_{22}N_4O_2$: C, 74.63; H, 5.10; N, 12.90. Found: C, 74.58; H, 5.09; N, 12.95). Structure X was assigned by analogy to the similar product V; in accordance with this structure, more drastic hydrolysis (24 hrs. treatment with boiling ethanolic KOH) of the above triazolidone m.p. 158-159° furnished, besides some unchanged product, benzophenone phenylsemicarbazone in 57 % yield and aniline hydrochloride in 51 % yield.

As far as the two examples here reported allow to generalize, the reaction between diazoalkanes and azodicarboxylic derivatives represents, provided some steric requirements are satisfied, a source of highly reactive azomethine imines.

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