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THE PYRAZOLE ANALOGUE OF ORTHO-QUINODIMETHANE : GENERATION AND CYCLOADDITION REACTIONS

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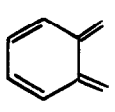
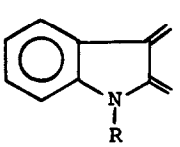
SUMMARY: The hitherto unknown 1-benzoyl-4,5-dihydro-4,5-dimethylene-3-phenyl-1*H*-pyrazole (the pyrazole analogue of ortho-quinodimethane) has been generated in solution and trapped with symmetrical and unsymmetrical dienophiles.

ortho-Quinodimethane (**1**) and indole-2,3-quinodimethane (**2**) have found wide application in the synthesis of natural products.[1-3] In addition, although there has been recently a considerable increase in the number of reports describing generation procedures and the reactivity of 5-membered heterocyclic analogues of ortho-quinodimethane (**1**) they are largely limited to furan- (**3**) and thiophene-2,3-quinodimethanes (**4**) and their benzo-derivatives.[4,5]

Very recently Storr and coworkers reported[6] the generation by flash pyrolysis of thiazole- (**5**), oxazole- (**6**) and 1-methylimidazole-4,5-quinodimethanes (**7**). However, co-condensation with methyl acrylate leading to a Diels-Alder adduct was successful only in the case of oxazole-4,5-quinodimethane (**6**). In addition, all their attempts to make by flash pyrolysis the 1-phenylpyrazole-4,5-quinodimethane as well as the isomeric pyrazole-3,4-quinodimethane failed. This report prompted us to disclose our results concerning the generation and intermolecular cycloaddition with symmetrical and unsymmetrical dienophiles of 1-benzoyl-4,5-dihydro-4,5-dimethylene-3-phenyl-1*H*-pyrazole (**10**).



1



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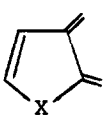
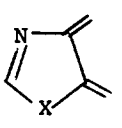


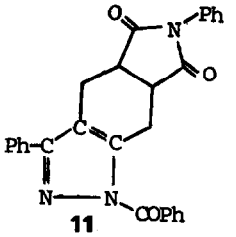
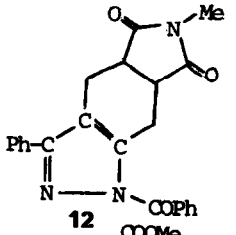
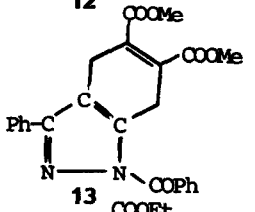
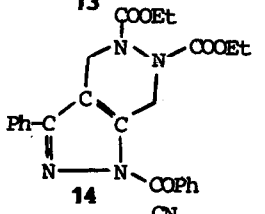
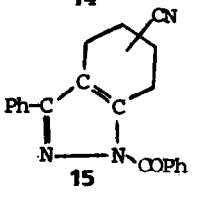
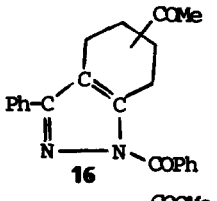
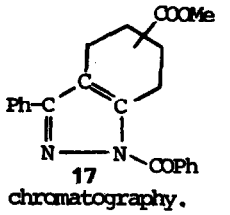
3, X = O
4, X = S



5, X = S
6, X = O
7, X = NMe

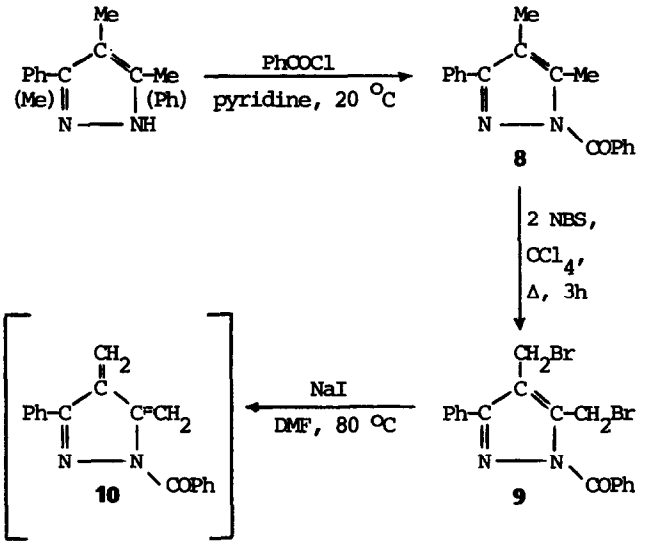
Our synthesis of **10** is shown in the Scheme. Benzoylation of 4,5-dimethyl-3-phenyl-1*H*-pyrazole[7] afforded the 1-benzoyl-4,5-dimethyl-3-phenyl-1*H*-pyrazole (**8**) (mp. 138-140 °C, 76% yield) as the only product[8], after chromatography (silica gel - petrol/ethyl acetate 20:1) of the crude reaction mixture. Bromination[9] of **8** gave the 1-benzoyl-4,5-bis(bromomethyl)-pyrazole **9** in 78% yield (mp. 96-98 °C, ether) after conventional work up. By 1,4 elimination of bromine, achieved[10] by treatment of the bis-bromide **9** with sodium iodide in DMF

TABLE: Diels-Alder Reactions of Pyrazole-4,5-quinodimethane **10** with Dienophiles

Dienophile	Cycloadduct	Yield[a] % (ratio)
N-Phenylmaleimide	 **11**	52
N-Methylmaleimide	 **12**	51
Dimethyl acetylene-dicarboxylate	 **13**	29
Diethyl azodicarboxylate	 **14**	54
Acrylonitrile	 **15**	39 (1:2.6)
Methyl vinyl ketone	 **16**	31 (1:1.5)
Methyl acrylate	 **17**	38 (1:1.4)

[a]Isolated yields after column chromatography.

at 80-90 °C, the pyrazole-4,5-quinodimethane **10** was generated which was trapped as its Diels-Alder adducts[11] in reasonable yields (Table). Some polymeric material was also formed.



Scheme

When **10** was trapped *in situ* with the unsymmetrical dienophiles, acrylonitrile, methyl vinyl ketone or methyl acrylate, mixtures of the two possible regioisomers were obtained[12], which were homogeneous on TLC. However, the presence of the two regioisomers was revealed by ^{1}H and ^{13}C NMR. In the absence of the dienophile only polymeric material was isolated. The high propensity of the pyrazole-4,5-quinodimethane system towards preferential polymerization, even in the presence of dienophiles, most probably accounts for the obtained cycloadduct yields (30-55%).

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11. Selected data for the new cycloadducts **11-14** are given. Compound **11**: Mp. 118-120 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.06-3.14(1H, m), 3.37-3.58(4H, m), 4.02-4.09(1H, m), 7.19-7.62(11H, m), 7.68-7.71(2H, m), 8.11-8.13(2H, m); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 21.00(CH_2), 23.00(CH_2), 38.92 (CH), 39.38(CH), 116.37(C-7a), 141.87(C-4a), 151.83(C-7), 167.60(N-COPh), 177.62(CO), 177.99 (CO). Compound **12**: Mp. 95-97 °C; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 2.91(3H, s, NMe), 3.19-3.51(4H, m, 2XCH_2), 3.80-4.21(2H, m, 2XCH), 7.29-7.74(8H, m, ArH), 8.00-8.21(2H, m, ArH). Compound **13**: Mp. 165-167 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.80(2H, t, J=7Hz, CH_2), 3.84(3H, s, Me), 3.85(3H, s, Me), 4.21(2H, t, J=7Hz, CH_2), 7.38-7.62(6H, m, ArH), 7.73-7.76(2H, m, ArH), 8.12-8.15(2H, m, ArH). Compound **14**: 144-146 °C; ^{1}NMR ($CDCl_3$, 80MHz) δ 1.26(6H, t, J=7Hz, 2XMe), 4.22(4H, q, J=7Hz, 2XCH_2CH_3), 4.52 and 5.62(2H, AX system, J_{AX}=18Hz, CH_2), 4.75 and 5.21(2H, AX system, J_{AX}=18Hz, CH_2), 7.25-7.74(8H, m, ArH), 8.12-8.33(2H, m, ArH); ^{13}C NMR ($CDCl_3$, 270 MHz) δ 14.51 (2XCH_3), 42.07(CH_2), 45.01(CH_2), 62.83(CH_2CH_3), 62.89(CH_2CH_3), 115.70(C-9), 140.16(C-8), 151.08(C-3), 155.22(2XCOOEt), 167.18(N-COPh). All compounds gave correct elemental analysis and a high intensity molecular ion in the mass spectra.
12. Selected data for the cycloadducts **15-17** isolated from the unsymmetrical dienophiles are given: Compound **15**: The two possible regioisomers were separated by fractional crystallization from ether in a ratio of 1:2.6. Major isomer: Mp. 84-85 °C; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 2.02-2.42(2H, m), 2.80-3.65(5H, m), 7.31-7.82(8H, m), 8.01-8.22(2H, m). Minor isomer: Mp. 113-115 °C; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.95-2.40(2H, m), 2.80-3.60(5H, m), 7.30-7.80(8H, m), 7.95-8.20(2H, m). Despite several attempts, we have not been successful in gaining structural information on major or minor isomer of **15** via X-ray crystallographic methods. Compound **16**: oil; mixture of the two possible regioisomers in a ratio of 1:1.5 as was deduced from the ^{1}H NMR where two singlets at δ 2.28 and 2.29 were observed for the COMe protons. Compound **17**: oil; mixture of the two possible regioisomers in a ratio of 1:1.4 as was deduced by the ^{13}C NMR and also the ^{1}H NMR where two singlets at δ 3.73 and 3.74 were observed for the COOMe protons. All compounds gave correct elemental analysis and a high intensity molecular ion in the mass spectra.

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