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1,3-Dipolar Cycloaddition Reaction of 1-Methylperimidine 3-Ylides with Dimethyl Acetylenedicarboxylate

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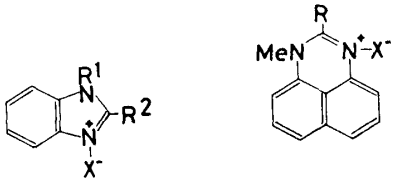
3-Amino-1-methylperimidinium mesitylenesulfonate reacted with dimethyl acetylenedicarboxylate (DMAD) in the presence of base to give dimethyl 1-(8-methylamino-1-naphthyl)pyrazole-3,4-dicarboxylate, whereas the reaction of the 2-methyl congener gave dimethyl 7-methyl-7*H*-benzo[*de*]pyrazolo[3,2-*b*]quinazoline-8,9-dicarboxylate as a major product. The reaction of 1-methyl-3-phenacyl- and 3-methoxycarbonylmethyl-perimidinium bromides with DMAD gave dimethyl 1-(8-methylamino-1-naphthyl)-2-benzoylpyrrole-3,4-dicarboxylate and trimethyl 1-(8-methylamino-1-naphthyl)pyrrole-2,3,4-tricarboxylate as major products, respectively.

Keywords——1,3-dipolar cycloaddition; 1-methylperimidine 3-ylides; dimethyl acetylenedicarboxylate; *O*-mesitylenesulfonylhydroxylamine

The 1,3-dipolar cycloadditions of 1-alkylbenzimidazole 3-ylides (**1**) have been well investigated and several unusual reactions have been observed.[1] It appeared to be of interest to compare the 1,3-dipolar character of the six-membered analogues, 1-alkylperimidine 3-ylides (**2**), with that of **1**. In this paper we wish to describe the reaction of the ylides **2** with dimethyl acetylenedicarboxylate (DMAD).

The starting 3-amino-1-methylperimidinium mesitylenesulfonates (**4a**, **b**) were prepared in good yields by the reaction of 1-methylperimidines (**3a**, **b**) with *O*-mesitylenesulfonylhydroxylamine (MSH)[2] in methylene chloride at room temperature.

Treatment of **4a** with DMAD in dimethylformamide in the presence of potassium carbonate at 40—50°C for 2 h gave a single product in 78% yield, and this was assigned the structure **7** from its spectral properties. The infrared (IR) spectrum ($CHCl_3$) of **7** showed an NH absorption band at 3410 cm^{-1} and a carbonyl band at 1730 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum showed a signal due to a pyrazole ring proton at δ 8.14, two methoxyl singlets at δ 3.86 and 3.98, a doublet at δ 2.64 (3H, J=5 Hz, NCH_3), a broad signal at δ 3.3—3.7 (NH) and a multiplet (6H) in the aromatic region. After treatment with deuterium oxide, the signal at δ 3.3—3.7 disappeared and the doublet at δ 2.64 became a singlet, suggesting the presence of an $NHCH_3$ group.



1: X=NH, NCOR′, CHCOR′ 2: X=NH, CHCOPh, CHCOMe

Chart 1

On the other hand, the reaction of the 2-methyl congener **4b** with DMAD gave a complex mixture from which the major product **8** was isolated in 60% yield by repeated column chromatography. The structure of **8** was confirmed by elemental analysis and by spectral evidence. Thus, the elemental analysis and mass spectrum (MS) (M^+ 337) of **8** indicated the molecular formula $C_{18}H_{15}N_3O_4$. The IR spectrum of **8** showed a strong carbonyl band at 1720 cm^{-1} but no NH absorption band. The NMR spectrum ($CDCl_3$) of **8** showed an NCH_3 singlet at δ 3.57, two methoxyl singlets at δ 3.92 and 3.97, and aromatic proton signals between δ 6.5 and 7.7.

For comparison, we also investigated the behavior of the 1-methylperimidine methylides

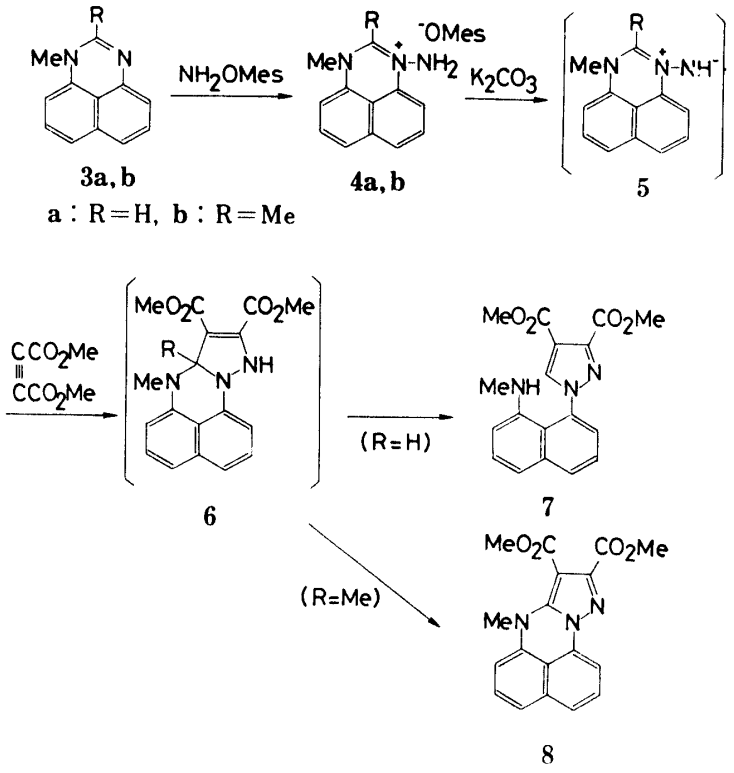


Chart 2

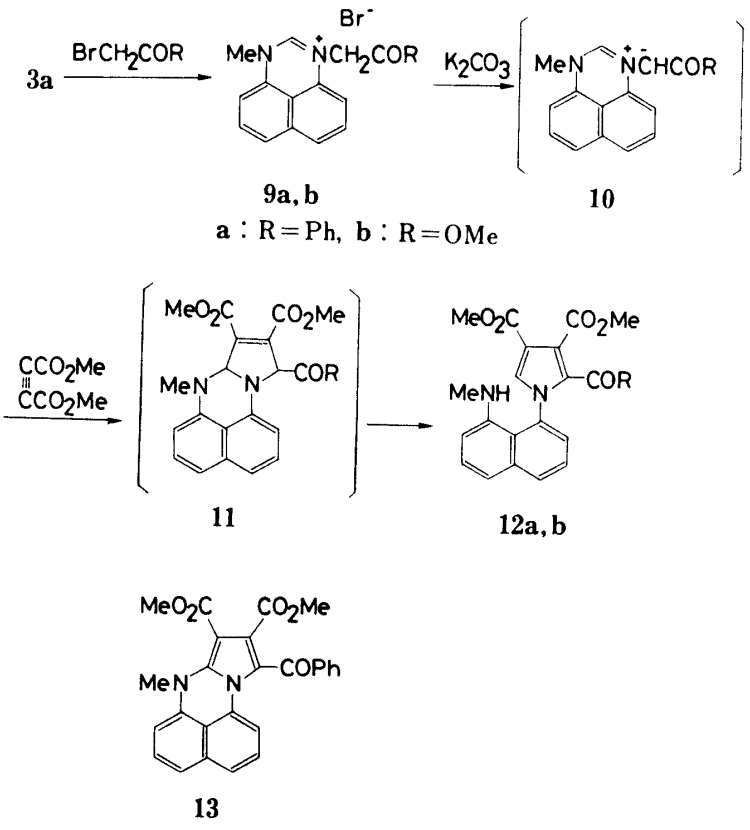


Chart 3

10. The precursors **9a, b** were prepared in 58 and 79% yields by the reaction of **3a, b** with phenacyl bromide and methyl bromoacetate, respectively. Reaction of **9a** with DMAD in the presence of potassium carbonate in dimethylformamide at 40—50°C gave a complex mixture, from which the major product **12a** was isolated by repeated column chromatography. The structure of **12a** was assigned on the basis of spectral evidence (see Experimental). The second major product was obtained as a mixture with **12a**, but the NMR spectrum of the mixture suggested the structure **13**: methoxyl singlets at δ 3.33 and 3.83 (overlapped with one of the methoxyl signals of **12a**) and an *N*-methyl singlet at δ 3.52.

Reaction of **9b** with DMAD gave a mixture of at least four products, from which a major product **12b** was obtained in a pure form by careful column chromatography. The structure of **12b** was defined by the spectral data (see Experimental).

Treatment of 1,2-dimethyl-3-phenancylperimidinium bromide with DMAD again gave a complex mixture which was not further investigated.

The formation of **7** and **12** presumably proceeds *via* 1,3-dipolar cycloaddition of initially formed ylides **5** (R=H) and **10** with DMAD followed by ring-opening of the primary adducts **6** (R=H) and **11**; this type of reaction has been observed in the reaction of 1-alkylbenzimidazole 3-ylides (**1**) with DMAD.[1] On the other hand, the formation of **8** from **4b** is rather unexpected because it requires the formal elimination of methane from the inetermediate **6** (R=Me). Such elimination of methane in the 1,3-dipolar cycloaddition has been reported only in the reaction of 3,6-dimethylpyridazine methoxycarbonylmethylide with DMAD.[3]

Experimental[4]

3-Amino-1-methylperimidinium (4a) and 3-Amino-1,2-dimethylperimidinium Mesitylenesulfonates (4b)——A solution of MSH (1.2 mmol) in methylene chloride (2 ml) was added dropwise to an ice-cooled solution of **3a**[5] (182 mg, 1 mmol) in methylene chloride (3 ml). The reaction mixture was stirred at room temperature for 2 h. The precipitated crystals were collected and recrystallized from ethanol to give **4a** (363 mg, 92%), mp 266—267°C. *Anal.* Calcd for $C_{21}H_{23}N_3O_3S$: C, 63.45; H, 5.83; N, 10.57. Found: C, 63.34; H, 5.78; N, 10.71.

Similar treatment of **3b**[5] (196 mg) gave **4b** (356 mg, 87%), mp 236—237°C. *Anal.* Calcd for $C_{22}H_{25}N_3O_3S$: C, 64.21; H, 6.08; N, 10.21. Found: C, 64.05; H, 6.11; N, 9.99.

Dimethyl 1-(8-Methylamino-1-naphthyl)pyrazole-3,4-dicarboxylate (7)——A mixture of **4a** (397 mg, 1 mmol), potassium carbonate (138 mg), and DMAD (213 mg, 1.5 mmol) in dimethylformamide (5 ml) was stirred at 40—50°C for 2 h. The mixture was filtered and filtrate was concentrated *in vacuo*. The residue was extracted with methylene chloride. The dried extract was concentrated and the residue was chromatographed on silica gel using benzene–ethyl acetate (5: 1) as the solvent to give **7** (264 mg, 78%), mp 101—102°C (from benzene–*n*-hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3410 (NH), 1730 (C=O). UV $\lambda_{max}^{ethanol}$ nm (log ε): 212 (4.71), 252 (4.45), 343 (3.84). NMR ($CDCl_3$) δ: 2.64 (3H, d, J=5 Hz, NCH_3), 3.3—3.7 (1H, br, NH), 3.86 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 6.5—6.7, 7.15—7.55 (6H, m, aromatic protons), 8.14 (1H, s, pyrazole ring proton). MS *m/e*: 339 (M^+). *Anal.* Calcd for $C_{18}H_{17}N_3O_4$: C, 63.71; H, 5.05; N, 12.38. Found: C, 63.81; H, 5.02; N, 12.37.

Dimethyl 7-Methyl-7*H*-benzo[*de*]pyrazolo[3,2-*b*]quinazoline-8,9-dicarboxylate (8)——The same procedure as that described above was used. Treatment of **4b** (411 mg, 1 mmol) with DMAD (213 mg, 1.5 mmol) gave many products, from which the major product **8** was isolated by repeated column chromatography on silica gel using benzene–ethyl acetate (3: 1) as the solvent; 333 mg (60%), mp 220—221°C (from benzene–*n*-hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO). UV $\lambda_{max}^{ethanol}$ nm (log ε): 221 (4.51), 253 (4.16), 31 6(3.90), 354 (3.91). NMR ($CDCl_3$) δ: 3.57 (3H, s, NCH_3), 3.92 (3H, s, OCH_3), 3.97 (3H, s, OCH_3), 6.5—6.7, 7.2—7.7 (6H, m, aromatic protons); MS *m/e*: 337 (M^+). *Anal.* Calcd for $C_{18}H_{15}N_3O_4$: C, 64.09; H, 4.48; N, 12.46. Found: C, 64.16; H, 4.30; N, 12.59.

1-Methyl-3-phenacylperimidinium Bromide (9a)——A mixture of **3a** (182 mg, 1 mmol) and phenacyl bromide (239 mg, 1.2 mmol) in acetone (5 ml) was allowed to stand at room temperature for 1 d. The precipitated crystals were collected and recrystallized from ethanol to give **9a**, 228 mg (58%) as pale orange needles, mp 258—259°C. *Anal.* Calcd for $C_{20}H_{17}BrN_2O \cdot 1/4H_2O$: C, 62.26; H, 4.70; N, 7.26. Found: C, 62.32; H, 4.81; N, 7.00.

1-Methyl-3-methoxycarbonylmethylperimidinium Bromide (9b)——A mixture of **3a** (182 mg, 1 mmol) and methyl bromoacetate (184 mg, 1.2 mmol) in acetone (5 ml) was allowed to stand at room temperature for 1 d. The precipitated crystals were collected and recrystallized from ethanol to give **9b** (265 mg, 79%) as reddish-brown crystals, mp 210—211°C. *Anal.* Calcd for $C_{20}H_{17}BrN_2O$: C, 53.71; H, 4.51; N, 8.36. Found:

C, 53.70; H, 4.43; N, 8.57.

Dimethyl 1-(8-Methylamino-1-naphthyl)-2-benzoylpyrrole-3,4-dicarboxylate (12a)——A mixture of **9a** (381 mg, 1 mmol), DMAD (213 mg, 1.5 mmol), and K_2CO_3 (138 mg, 1 mmol) in dimethylformamide (5 ml) was heated at 40—50°C under stirring for 5 h. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was extracted with chloroform and the extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel using benzene–ethyl acetate (1: 1) to give a mixture of **12a** and **13** (219 mg) in a ratio of *ca.* 3: 1. Rechromatography of a part of the mixture on silica gel using ether–*n*-hexane (3: 1) gave a pure sample of **12a**.

Compound **12a** had mp 168—169°C (from benzene–*n*-hexane). IR ν_{max}^{KCl} cm^{-1}: 3450 (NH), 1730, 1640 (CO). UV $\lambda_{max}^{ethanol}$ nm (log ε): 213 (4.54), 251 (4.29), and 340 (3.72). NMR ($CDCl_3$) δ: 2.73 (3H, d, J=5 Hz, NCH_3), 3.31 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.6 (1H, br, NH). *Anal.* Calcd for $C_{26}H_{22}N_2O_5$: C, 70.58; H, 5.01; N, 6.33. Found: C, 70.63; H, 4.88; N, 6.25.

The NMR spectrum of the mixture of **12a** and **13** showed signals of **13** at δ 3.33 (s, OCH_3), 3.52 (s, NCH_3), and 3.83 (s, OCH_3, overlapped with that of **12a**).

Trimethyl 1-(8-Methylamino-1-naphthyl)pyrrole-2,3,4-tricarboxylate (12b)——A similar procedure to that described above was used. Reaction of **9b** (335 mg, 1 mmol) with DMAD (213 mg, 1.5 mmol) gave a mixture of at least four products from which the major product **12b** was obtained in 52% yield by column chromatography on silica gel using ether–benzene (1: 10), as an oil which solidified on standing in a refrigerator but remelted at room temperature. IR ν_{max}^{KCl} cm^{-1}: 3480 (NH), 1755, 1740, 1720 (CO). UV $\lambda_{max}^{ethanol}$ nm (log ε): 216 (4.72), 253 (4.45), 344 (3.90). NMR ($CDCl_3$) δ: 2.64 (3H, d, J=4 Hz, NCH_3), 3.50, 3.80, 3.97 (3H each, s each, 3×OCH_3), 6.4—7.9 (7H, m, aromatic protons). Exact MS *m/e*: Calcd for $C_{21}H_{20}N_2O_6$, 396.1318; Found, 396.1316.

References and Notes

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