RING CLOSURE REACTIONS OF ADDUCTS OF METHACRYLOYL ISOCYANATE TO ARYLHYDRAZINES AND THEIR RELATED COMPOUNDS

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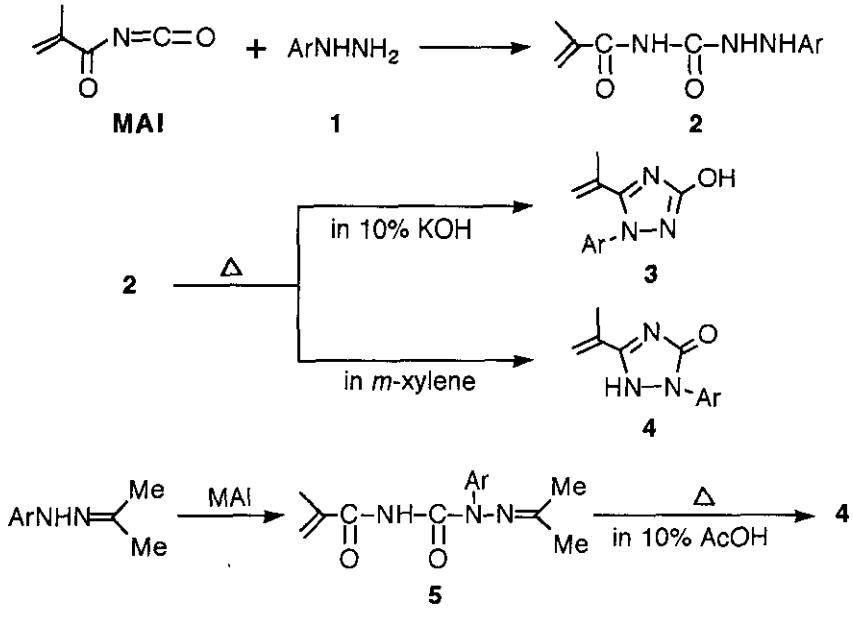
Abstract - Methacryloyl isocyanate (**MAI**) reacted with arylhydrazines (**1**) to give semicarbazides (**2**) in good yields. Treatment of **2** with aqueous potassium hydroxide gave the corresponding 1-aryl-3-hydroxy-1,2,4-triazoles (**3**), whereas thermal ring closure of **2** afforded isomeric 2,3-dihydro-2-aryl-1,2,4-triazole-3(1*H*)-ones (**4**). **MAI** reacted with benzamidine to give directly 1,3,5-triazine-2(1*H*)-one (**10**) by the loss of water. On the other hand, the reaction of **MAI** with 1,3-diphenylguanidine afforded the 1:1 adduct (**11**), which on thermal decomposition gave the perhydropyrimidin-6(1*H*)-one (**12**) and perhydro-1,3,5-triazine-2,6-dione (**13**). The pathways for the formation of **4**, **12** and **13** are also described.

Methacryloyl isocyanate (**MAI**) is a versatile polyfunctional reagent bearing an enone moiety as well as a highly reactive acyl isocyanato group.[1]

Nucleophilic additions to acyl isocyanates are popular and widely used reactions,[2] but a few examples have been reported for **MAI**.[1b,3] We have previously reported that on treatment with aqueous potassium hydroxide or hydrochloric acid, the semicarbazides prepared from benzoyl isocyanate and arylhydrazines underwent ring closure to 1-aryl-3-hydroxy-5-phenyl-1,2,4-triazoles, whereas thermal ring closure gave isomeric 2,3-dihydro-2-aryl-5-phenyl-1,2,4-triazol-3(1*H*)-ones, whose formation pathway was not clarified.[4]

We report here ring closure reactions of the adducts of **MAI** to arylhydrazines and their related compounds.

MAI readily reacted with phenyl- (**1a**), *p*-tolyl- (**1b**) and *p*-nitrophenylhydrazine (**1c**) to give the corresponding semicarbazides (**2a-2c**) in good yields, respectively.[5] Treatment of **2a** with a 10% aqueous potassium hydroxide under reflux for 4 h gave a normal cyclization product, 3-hydroxy-5-isopropenyl-1-phenyl-1,2,4-triazole (**3a**), mp 221-222 °C, in 73% yield. Although under similar conditions **2b** gave the corresponding triazole (**3b**), mp 254-255 °C, in 52% yield, intractable red tarry material was formed from **2c** (Scheme 1). Structural elucidation of the triazoles (**3**) was performed by spectral data.[6]



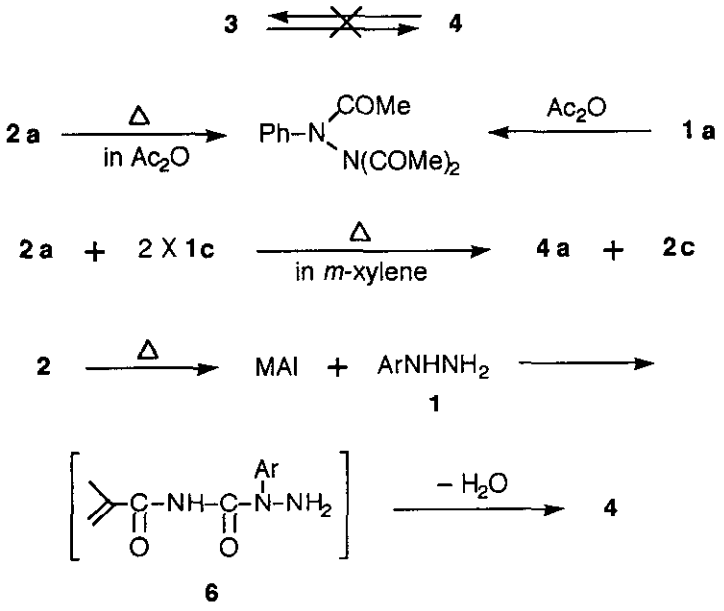
a : Ar = Ph ; **b** : Ar = *p*-MeC_6H_4 ; **c** : Ar = *p*-$NO_2C_6H_4$

Scheme 1

On the other hand, the thermal ring closure of semicarbazides (**2a**) and (**2b**) in refluxing *m*-xylene for 12 h afforded the corresponding 2,3-dihydro-2-aryl-5-isopropenyl-1,2,4-triazole-3(1*H*)-ones (**4a**), mp 173-174 °C, and (**4b**), mp 187-188 °C, in 76 and 55% yields, respectively. Under the same conditions, however, *p*-nitro derivative (**2c**) suffered no ring closure to the corresponding triazolinone (**4c**), but instead was recovered quantitatively. The structure of **4a** was confirmed by spectral data[6] as well as by direct comparison with an authentic sample prepared in 72% yield from the adduct (**5a**) as shown in Scheme 1. The *p*-nitro derivative (**4c**),

mp 219-220 °C, could be also prepared in 80% yield from the adduct (**5c**), mp 139-140 °C.

Several experiments were done in order to obtain information on the pathway for the formation of triazolinone (**4**) from semicarbazide (**2**). No thermal interconversion between **3** and **4** was observed. Heating of the semicarbazide (**2a**) in acetic anhydride for 1 h gave neither **3a** nor **4a**, but triacetylphenylhydrazine which was identical with an authentic sample prepared from acetylation of the hydrazine (**1a**), was isolated in 76 % yield. When **2a** was heated with two equimolar amounts of the hydrazine (**1c**) in refluxing *m*-xylene for 12 h, the triazolinone (**4a**) and thermally stable semicarbazide (**2c**) were obtained in 56 and 5.8% yields, respectively, together with recovery (76%) of **1c**. The latter two facts strongly indicate that semicarbazide (**2**) thermally dissociate into two original components, **MAI** and hydrazine (**1**). On the basis of the above observations, the pathway for thermal conversion of **2** to **4** can be viewed as illustrated in Scheme 2.

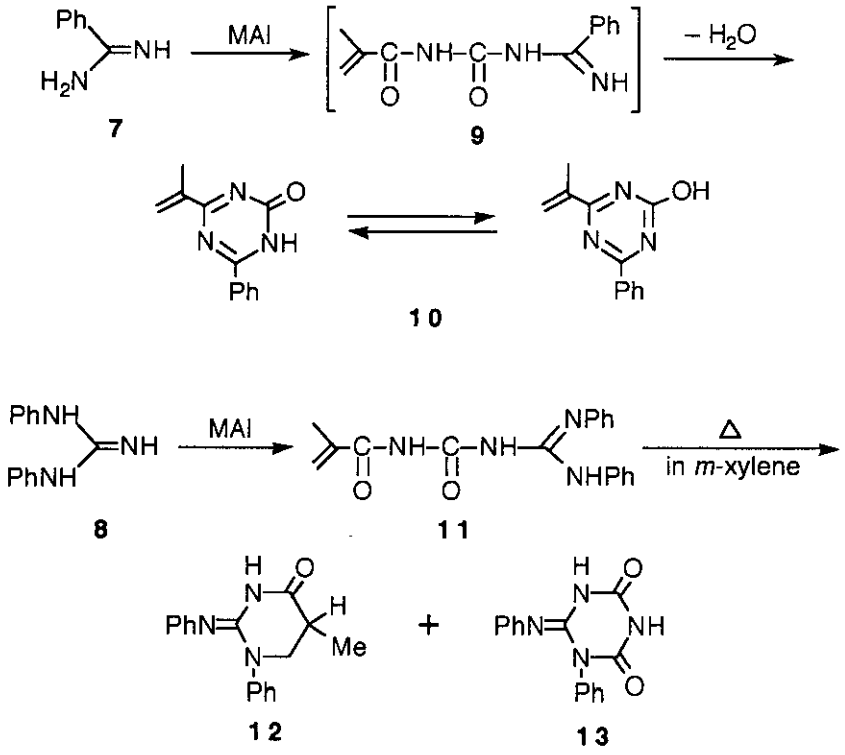


Scheme 2

Thus, semicarbazide (**2**) dissociates into **MAI** and hydrazine (**1**), followed by the recombination of **MAI** to α-nitrogen atom of **1** to yield 2-aryl-4-methacryloylsemicarbazide (**6**), which gives **4** by the loss of water. Even if thermal dissociation into **MAI** and **1c** occurred in the case of **2c**, the corresponding semicarbazide (**6c**) would not form owing to the low nucleophilicity of α–nitrogen atom in **1c**; thus thermal reaction of **2c** gives no **4c**. It

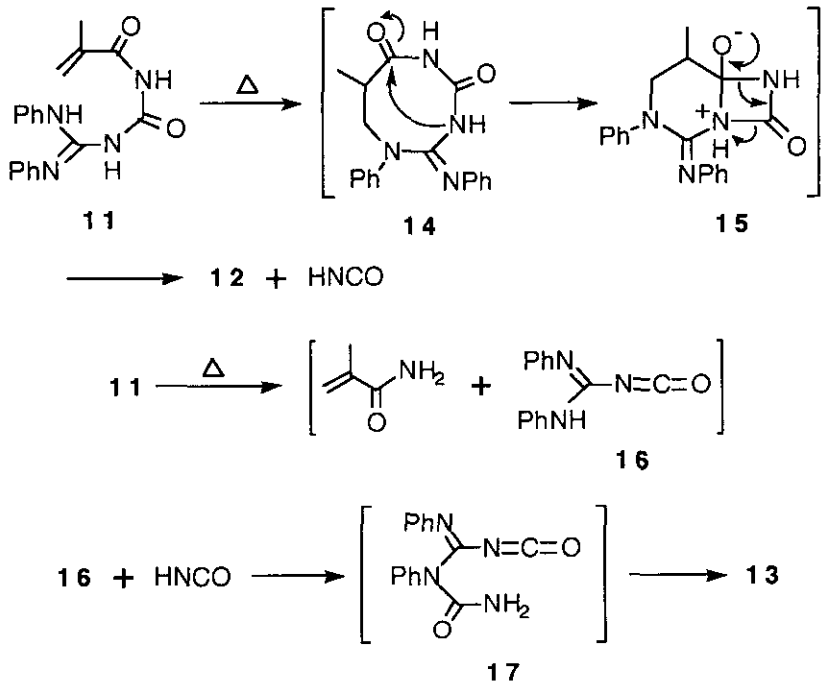
can be also considered that the thermal ring closure[4] of semicarbazides from benzoyl isocyanate proceeds in a similar manner as above.

Next, the reaction of **MAI** with benzamidine (**7**) and 1,3-diphenylguanidine (**8**) was studied. **MAI** was reacted with **7** in acetonitrile at 16 °C for 1 h to give directely a 54% yield of 1,2-dihydro-4-isopropenyl-6-phenyl-1,3,5-triazine-2(1*H*)-one (**10**)[7] *via* the unisolable adduct (**9**). On the other hand, in the reaction of **MAI** with **8**, the adduct, 1,2-diphenyl-3-methacryloylcarbamoylguanidine (**11**),[8] was isolated in 91% yield. Thermolysis of **11** in *m*-xylene under reflux for 6 h afforded two products (**12**) and (**13**) in 61 and 12% yields, respectively. The molecular formula of **12** corresponded to that of the compound derived from **11** by the elimination of isocyanic acid, whereas **13** had the molecular formula corresponded to that of the compound derived from **11** by the loss of propene. It is worth noting that any vinyl moiety is not present in both **12** and **13**. On the basis of spectral data, **12** and **13** were assumed to be perhydro-5-methyl-3-phenyl-2-phenyliminopyrimidin-6(1*H*)-one, and perhydro-3-phenyl-4-phenylimino-1,3,5-triazine-2,6-dione, respectively[9] (Scheme 3).



Scheme 3

The formation pathways for **12** and **13** might be viewed as shown in Scheme 4. An intramolecular Michael addition of **11** gives the eight-membered intermediate (**14**). Then, the elimination of isocyanic acid from **14** *via* the bicyclic betaine (**15**) affords stable **12**. The adduct (**11**) undergoes an alternative thermal decomposition into methacrylamide and isocyanate intermediate (**16**). Isocyanic acid eliminated from **14** adds to **16** to yield **17**, whose intramolecular cyclization produces **13**.



Scheme 4

Synthetic potential of the reaction of **MAI** with other bifunctional active hydrogen compounds is being further investigated.

ACKNOWLEDGEMENTS

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5. **MAI** reacted with an equimolar amount of **1** in THF at 0 °C to give the corresponding semicarbazide: **2a**, mp 184-185 °C (decomp.), **2b**, mp 169-170 °C (decomp.), and **2c**, mp 219-220 °C (decomp.), were obtained in 77, 80 and 93% yields, respectively. For example, spectral data of **2a** are as follows: Ir (KBr) 3294, 3228, 1678 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.97 (3H, d, J=1.5 Hz, C**H**$_3$), 5.40 (1H, q, J=1.5 Hz, =C**H**), 5.80 (1H, s, =C**H**), 5.99 (1H, br s, PhN**H**), 6.66-7.43 (5H, m, Ar**H**), 9.04 (1H, br s, CON**H**CO), 10.04 (1H, br s, PhNHN**H**); ms m/z 219 (M^+).

   All new compounds in this paper gave satisfactory elementary analyses.

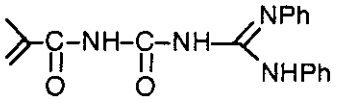
6. For example, spectral data of **3a** and **4a** are shown. **3a**: Ir (KBr) 2548 (OH), 1576 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.00 (3H, s, C**H**$_3$), 5.27, 5.33 (each 1H, s, =C**H**), 7.37 (5H, s, Ar**H**), 8.83 (1H, s, O**H**); ^{13}C nmr (DMSO-d_6) δ 21.03, 120.86, 125.37, 128.54, 129.28, 132.23, 138.20, 152.76, 166.03; ms m/z 201 (M^+). **4a**: Ir (KBr) 3150 (NH), 1715 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.13 (3H, s, C**H**$_3$), 5.38, 5.73 (each 1H, s, =C**H**), 7.00-7.59 (3H, m, Ar**H**), 7.76-8.17 (2H, m, Ar**H**), 12.66 (1H, br s, N**H**); ^{13}C nmr ($CDCl_3$) δ 17.78; 118.06, 119.16, 125.61, 128.93, 130.84, 137.69, 146.49, 154.80; ms m/z 201 (M^+).

7. Nmr spectra indicated that **10**, mp 177-178 °C (decomp.), exists in the corresponding enol form, 2-hydroxy-1,3,5-triazine in solution. Ir (KBr) 3218, 3110, 1671 cm^{-1}; ^1H nmr (DMSO-d_6) δ 2.15 (3H, s, C**H**$_3$), 5.87, 6.52 (each 1H, s, =C**H**), 7.41-7.90 (4H, m, Ar**H** + O**H**), 8.20-8.48 (2H, m, Ar**H**); ^{13}C nmr (DMSO-d_6) δ 18.51, 125.52, 128.66, 133.02, 133.68, 138.54, 157.08, 168.63, 169.30; ms m/z 213 (M^+).

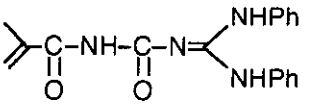
8. Three structures, **11A**, **11B** and **11C**, are possible for the adduct of **MAI** to **8**. On the basis of the comparison of spectral data with those of related compounds, **2a** (see ref. 5), *N,N'*-diphenylformamidine (N**H** (δ 7.40)) and **8** (=N**H** (δ 5.19), PhN**H** (6.7–7.0)), **11** was assigned as **11A**.

   11: mp 175-176 °C; ir (KBr) 3300, 3281, 3148, 1698, 1663 cm^{-1}; ^1H nmr (DMSO-d_6) δ 1.78 (3H, s, C**H**$_3$), 5.63, 5.90 (each 1H, s, =C**H**), 6.70-7.90 (11H, m, Ar**H** + PhN**H** (δ 7.65)), 9.89 (1H, br s,

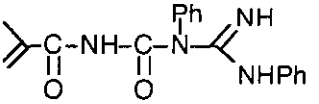
CONHCO), 10.68 (1H, br s, CONHC=N); ^{13}C nmr (DMSO-d_6) δ 17.90, 121.37, 121.55, 121.83, 122.50, 124.41, 128.25, 128.89, 137.64, 139.84, 152.26, 152.46, 169.64; ms m/z 322 (M^+).



11A



11B



11C

9. **12**: mp 175-176 °C; ir (KBr) 3300, 3190, 1694 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.31 (3H, d, J=7.0 Hz, C**H**$_3$), 2.89 (1H, ddq, J=7.0, 9.0, 9.0 Hz, 5-**H**), 3.65 (1H, dd, J=9.0, 12.5 Hz, 4-**H**), 3.88 (1H, dd, J=7.0, 12.5 Hz, 4-**H**), 6.80-8.20 (11H, m, Ar**H** + N**H**); ^{13}C nmr (DMSO-d_6) δ 12.49, 35.52, 52.63, 119.37, 122.58, 125.87, 128.56, 128.75, 128.84, 138.97, 143.33, 147.59, 162.03; ms m/z (rel. int., %) 279 (M^+), 278 (100), 236 (M^+ - HNCO, 63). **13**: mp 248-249 °C (decomp.); ir (KBr) 3375, 3178, 1736, 1692 cm^{-1}; ^{1}H nmr (DMSO-d_6) δ 7.20-7.30 (5H, m, Ar**H**), 7.53 (5H, s, Ar**H**), 8.22, 11.00 (each 1H, br s, N**H**); ^{13}C nmr (DMSO-d_6) δ 125.53, 128.01, 129.54, 129.78, 133.09, 136.94, 150.53, 154.69, 154.84; ms m/z (rel. int.,%) 280 (M^+), 279 (100), 236 (279^+ - HNCO, 22), 119 ([PhNCO]$^+$, 16).

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