

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

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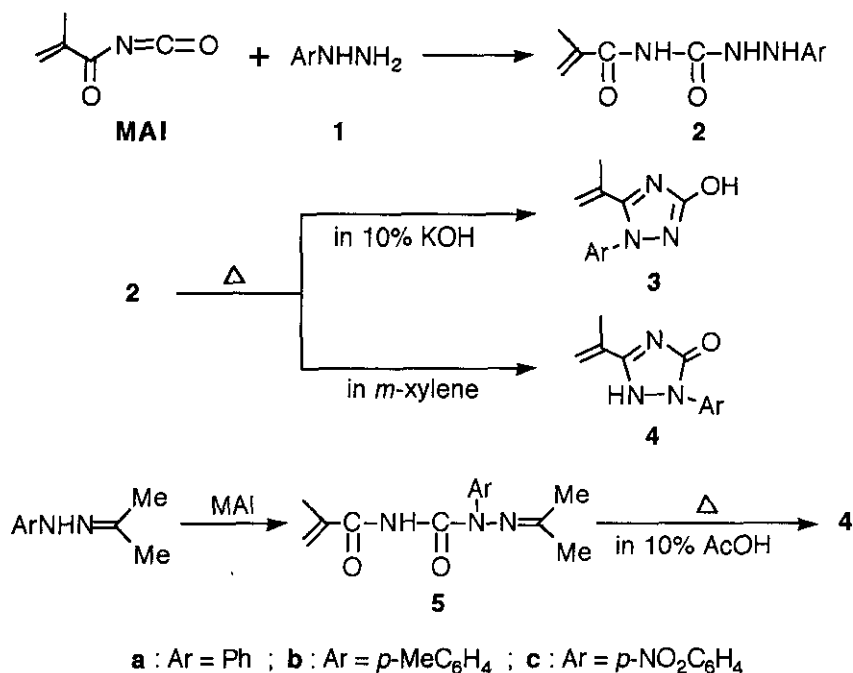
Abstract - Methacryloyl isocyanate (**MAI**) reacted with arylhydrazines (**1**) to give semicarbazides (**2**) in good yields. Treatment of **2** with aqueous potassium hydroxide gave the corresponding 1-aryl-3-hydroxy-1,2,4-triazoles (**3**), whereas thermal ring closure of **2** afforded isomeric 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

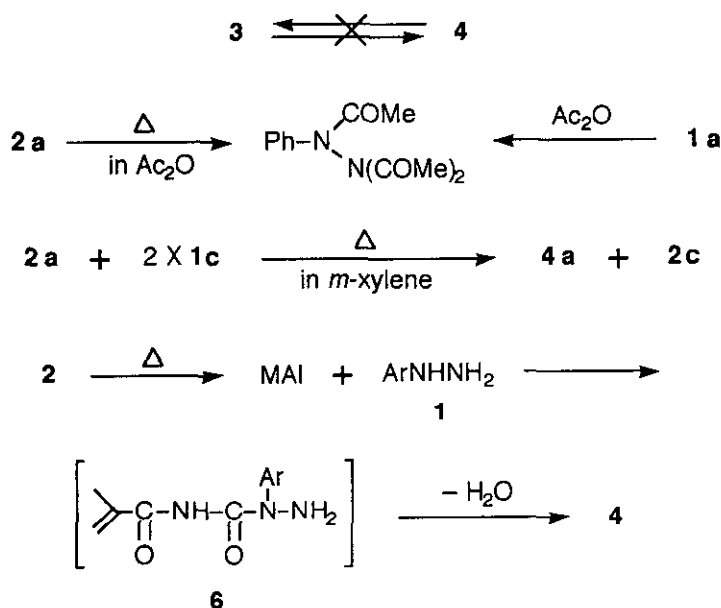


Scheme 1

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 data⁶ 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.

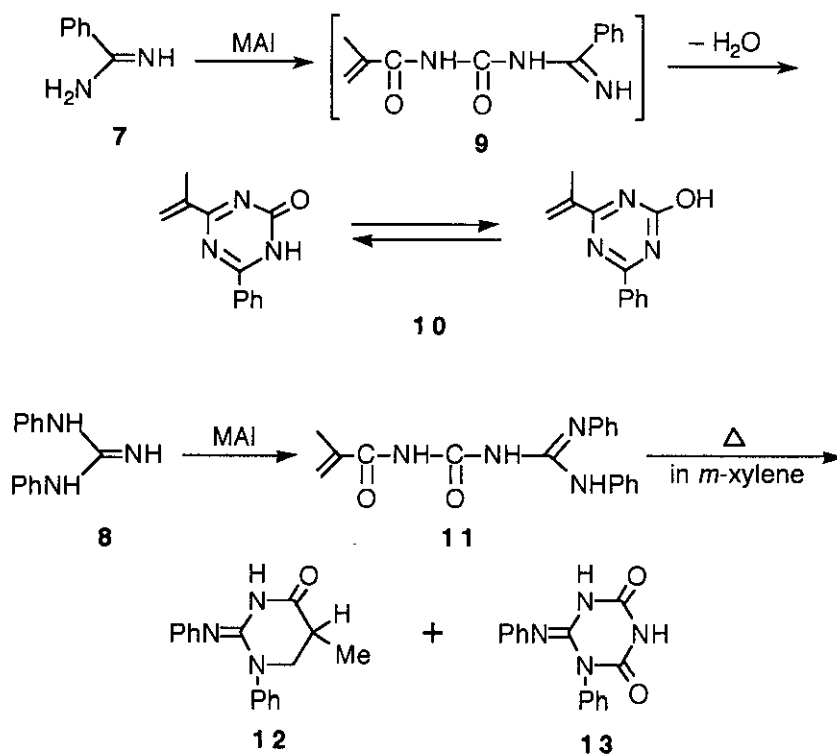


Scheme 2

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

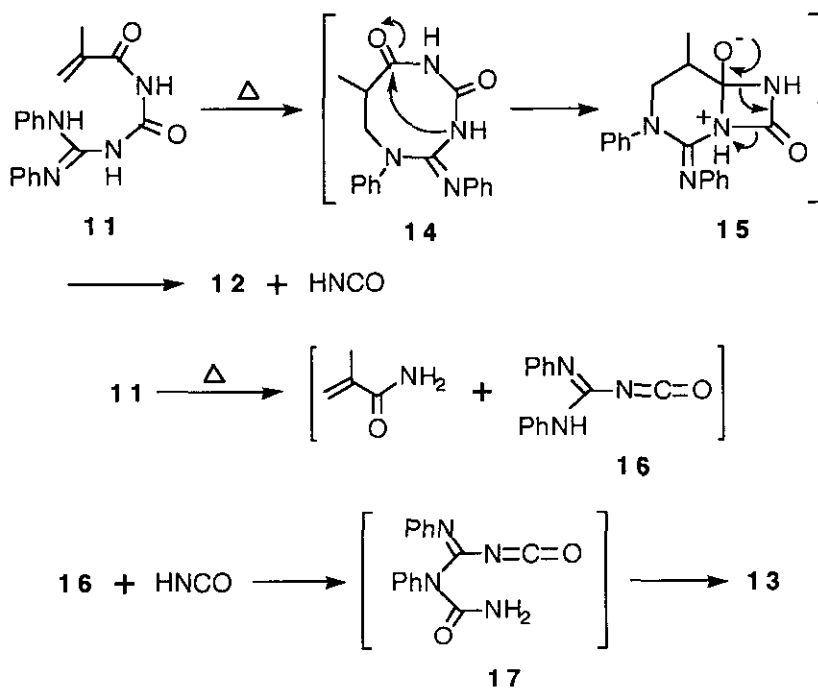
can be also considered that the thermal ring closure⁴ of semicarbazides from benzoyl isocyanate proceeds in a similar manner as above.

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 directly 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, respectively⁹ (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.

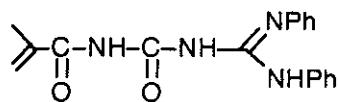
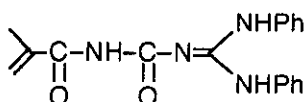
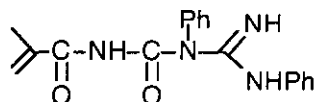
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5. MAI reacted with an equimolar amount of **1** in THF at 0 °C to give the corresponding semicarbazide: **2a**, mp 184-185 °C (decomp.), **2b**, mp 169-170 °C (decomp.), and **2c**, mp 219-220 °C (decomp.), were obtained in 77, 80 and 93% yields, respectively. For example, spectral data of **2a** are as follows: Ir (KBr) 3294, 3228, 1678 cm⁻¹; ¹H nmr (CDCl₃) δ 1.97 (3H, d, J=1.5 Hz, CH₃), 5.40 (1H, q, J=1.5 Hz, =CH), 5.80 (1H, s, =CH), 5.99 (1H, br s, PhNH), 6.66-7.43 (5H, m, ArH), 9.04 (1H, br s, CONHCO), 10.04 (1H, br s, PhNHNH); 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 (CDCl₃) δ 2.00 (3H, s, CH₃), 5.27, 5.33 (each 1H, s, =CH), 7.37 (5H, s, ArH), 8.83 (1H, s, OH); ¹³C nmr (DMSO-d₆) 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 (CDCl₃) δ 2.13 (3H, s, CH₃), 5.38, 5.73 (each 1H, s, =CH), 7.00-7.59 (3H, m, ArH), 7.76-8.17 (2H, m, ArH), 12.66 (1H, br s, NH); ¹³C nmr (CDCl₃) 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-d₆) δ 2.15 (3H, s, CH₃), 5.87, 6.52 (each 1H, s, =CH), 7.41-7.90 (4H, m, ArH + OH), 8.20-8.48 (2H, m, ArH); ¹³C nmr (DMSO-d₆) 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 (NH (δ 7.40)) and **8** (=NH (δ 5.19), PhNH (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-d₆) δ 1.78 (3H, s, CH₃), 5.63, 5.90 (each 1H, s, =CH), 6.70-7.90 (11H, m, ArH + PhNH (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} ; ^1H nmr (CDCl_3) δ 1.31 (3H, d, $J=7.0$ Hz, CH_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, ArH + NH); ^{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 ($M^+ - \text{HNCO}$, 63). **13**: mp 248-249 °C (decomp.); ir (KBr) 3375, 3178, 1736, 1692 cm^{-1} ; ^1H nmr (DMSO- d_6) δ 7.20-7.30 (5H, m, ArH), 7.53 (5H, s, ArH), 8.22, 11.00 (each 1H, br s, NH); ^{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 ($279^+ - \text{HNCO}$, 22), 119 ($[\text{PhNCO}]^+$, 16).

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