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A REINVESTIGATION OF THE REACTIONS BETWEEN DIAZOMETHANE AND 1-PHENYLURAZOLE

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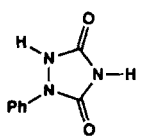
Exhaustive methylation of 1-phenylurazole (1), using ethereal diazomethane as the methylating agent, results in the formation of three products: 1-phenyl-3,5-dimethoxy-1,2,4-triazole (2), 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one (3) and 1-phenyl-2,4-dimethylurazole (4). Based on the amounts of 2–4 isolated, the overall yields in these reactions are typically >90%. When 1 and diazomethane were allowed to react in a fashion that resulted in the formation of monomethylated analogues of 1, 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (5) and 1-phenyl-2-methylurazole (6) were formed. In separate experiments, the monomethylated species 5 and 6 were allowed to react with diazomethane in efforts to develop a sequence of reactions that reasonably accounts for the formation of 2–4. Whereas *N*- and *O*-methylated products were obtained when 5 was treated with ethereal diazomethane, the reaction of 6 and diazomethane produced only the *N*-alkylated product 1-phenyl–2,4-dimethylurazole (in quantitative yield). The outcomes of these experiments are consistent with a sequence of reactions in which the treatment of 1 with diazomethane results, initially, in the formation of the monomethylated species 5 and 6. In the presence of sufficient diazomethane, 5 and 6 then undergo further methylation, forming the dimethylated species 2–4.

INTRODUCTION

In the course of carrying out research aimed at evaluating and understanding various aspects of the proton, electron, and hydrogen atom transfer chemistry of urazole and substituted urazoles[1,2] such as 1-phenylurazole (1-phenyl-1,2,4-triazolidine-2,4-dione) (**1**), we found it necessary to synthesize *O*-methylated heterocycles such as 1-phenyl-3,5-dimethoxy-1,2,4-triazole (**2**) and 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one (**3**). Published literature as well as our own experience suggested that treatment of **1** with electrophiles such as dimethyl sulfate[3] and methyl iodide[4] would not result in the transformation of **1** into **2** and/or **3**, since these reagents, when allowed to react with substituted urazoles, have been shown to generally result in the formation of *N*-methylated analogues of **1**. However, it has been demonstrated that treatment of variously substituted urazoles with diazomethane results in the O-methylation of the urazole substrates.[3,5,6,7]



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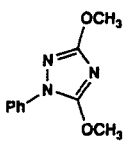

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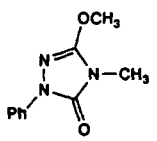

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For example, in a recent summary, it was stated that the reaction of 1-phenylurazole (**1**) and diazomethane 'gives 1-phenyl-3-methoxy-4-methylurazole (i.e. 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one)' (**3**).[8] An older review also stated that the reaction of **1** and diazomethane results in the formation of **3**, but also noted that other *N*- and *O*-methylated compounds were formed.[5] Both of these reviews are based (in part) on experiments carried out by Acree in 1907, who also stated that 'traces of other dimethyl derivatives'[3] are formed in these reactions.

In our laboratories, we allowed 1-phenylurazole (and also other variously substituted urazoles) to react with diazomethane, under various reaction conditions. Our results are significant in that some of the products isolated after diazomethane had been allowed to react with the urazoles differ in certain respects from those reported previously.[3,5,6,8] In this paper, we describe the composition of the products isolated in these reactions and propose a likely path for their formation.

RESULTS

In our laboratory, we find that 1-phenylurazole (**1**), when exhaustively methylated with diazomethane under

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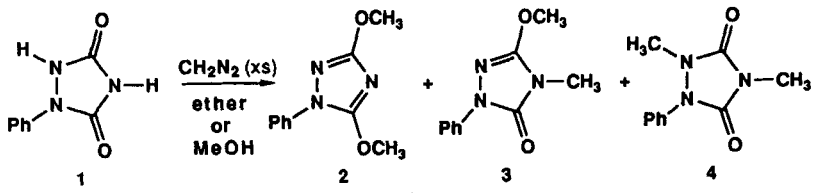


1 2 3 4 (1)

Protocol	% Yield	% Yield	% Yield	Total Yield
A	24	34	38	96
B	25	33	28	86
C	20	32	46	98
D	18	35	46	99

any of four different reaction conditions (protocols A, B, C and D), forms (di-*O*-methylated) 1-phenyl-3,5-dimethoxy-1,2,4-triazole (**2**), in addition to 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one (**3**) and (di-*N*-methylated) 1-phenyl-2,4-dimethylurazole (**4**). As shown in equation (1), **2**–**4** were isolated in combined yields generally greater than 90%, for reactions carried out four different ways (protocol A, solid 1-phenylurazole was added to ethereal diazomethane; protocol B, an ethereal solution of diazomethane was added in portions to a suspension of ethereal 1-phenylurazole; protocol C, a methanolic solution of 1-phenylurazole was added to an ethereal solution of diazomethane; and protocol D, an ethereal solution of diazomethane was added slowly to a methanolic solution of 1-phenylurazole). Inspection of the yields listed below equation (1) reveals that greater than 50% of the products isolated after **1** had been allowed to react with diazomethane (i.e. **2** and **4**) are different to the species previously identified as the primary reaction product (i.e. **3**).

Production isolation and identification

Chromatographic and spectroscopic techniques not available to earlier chemists were utilized in our efforts to isolate and identify **2**–**4**. Separation of **2**–**4** from the crude reaction mixture is easily accomplished with the aid of preparative chromatography, using silica gel as the adsorbent and ethyl acetate–hexane as the eluent. NMR evidence aided in the characterization of **2**–**4**. That **3** possesses one —NCH_3 and one —OCH_3 moiety is supported by ^{1}H NMR signals at 3·09 and 4·03 ppm, signals assignable to the methyl protons present in —NCH_3 and —OCH_3, respectively. By analogy, signals in the proton spectrum of **2** (at 3·89 and 4·10 ppm) are assignable to the —OCH_3 protons in **2**, while signals present in the proton spectrum of **4** (at 2·99 and 3·02 ppm) are assignable to the —NCH_3 protons in **4**. ^{13}C NMR also provides evidence for these structural assignments, since the spectra for **2**, **3** and **4** possess signals at 56·4 and 59·4; 56·4 and 25·8; and 33·9 and 25·4 ppm, respectively. In addition, the IR spectrum for 1-phenyl-3,5-dimethoxy-1,2,4-triazole (**2**) possesses absorption bands consistent with the presence of triazolyl C=N bonds (1560 and 1580 cm^{-1}). Conspicuous by their absence in the IR spectrum of **2** are any absorptions in the 1700–1800 cm^{-1} region indicative of C=O bonds. On the other hand, evident in the IR spectra for **3** and **4** (both of which contain C=O moieties) are absorptions at 1722 cm^{-1} (**3**) and 1722 and 1786 cm^{-1} (**4**).

DISCUSSION

Our results differ substantially from those reported by Acree[3] in 1907, and referred to in subsequent years by Gompper[6] and Katritzky.[8] Without access to preparative-scale chromatographic techniques, it is easy to understand that Acree was unable to isolate a low-melting solid such as 1-phenyl-3,5-dimethoxy-1,2,4-triazole (**2**, m.p. 43–44 °C) from a reaction mixture that in all likelihood contained substantial amounts of two additional isometric products (**3** and **4**).

Nevertheless in efforts to compare our results with those published previously, we felt it was necessary to vary the conditions of the diazomethane–1-phenylurazole reactions, in the light of the regiochemical outcome of reactions in which diazomethane was allowed to react with ambient substrates. For example, when an ethereal solution of saccharin was added to an ethereal solution of diazomethane, 10% of the *O*-alkylated product (*O*-methylsaccharin) was formed in addition to the *N*-methyl derivative. However, if the order of addition is reversed (i.e. the diazomethane solution was added to a saturated ethereal solution of saccharin), the proportion of *O*-alkylated product increases to 24%.[9] In other words, selected amides 'are methylated principally on nitrogen if the amide is introduced into excess ethereal diazomethane, but principally on oxygen if the diazomethane is gradually dropped into the ethereal amide solution (or suspension).'[10]

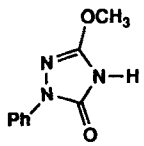
Examination of the yield data for the reaction shown

in equation (1) reveals that **2–4** were isolated, in substantial amounts, regardless of whether 1-phenylurazole was added to ethereal diazomethane (protocols A and C), or ethereal diazomethane was added to 1-phenylurazole (protocols B and D). It is unlikely that the differences between the products isolated in this work and those isolated by Acree (using protocol B) are the result of differences in reaction conditions.

Monomethylated 1-phenylurazoles

It was therefore incumbent upon us to outline a reaction pathway that reasonably accounts for the formation of dimethylated species **2**, **3** and **4** resulting from diazomethane-induced exhaustive methylation of **1**. Crucial to a complete analysis of the reaction pathway is an understanding of the regiochemistry of the initial diazomethane-induced monomethylation of 1-phenylurazole.

Five monomethylated analogues of 1-phenylurazole are shown (**5–9**). Described in Ref. 3 are results from



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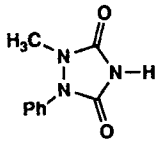

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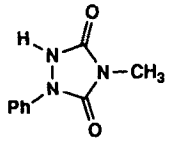

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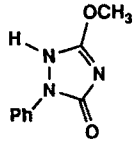

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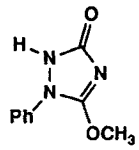

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an experiment in which ethereal diazomethane was added to excess 1-phenylurazole. In this reaction, 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (**5**) was thought to be the chief product [along with a small amount of 1-phenyl-2-methylurazole (**6**)]. The monomethylated species 1-phenyl-4-methylurazole (**7**), 1-phenyl-3-methoxy-Δ^3-1,2,4-triazolin-5-one (**8**)* and 1-phenyl-5-methoxy-Δ^4-1,2,4-triazolin-3-one (**9**) were not isolated in this reaction,[3] nor have **7–9** ever been observed,[1–7,9b] either as intermediates or products, in any reaction in which 1-phenylurazole has been allowed to react with diazomethane.

We have completed two experiments in which we investigated the monomethylated analogues of **1** formed when **1** is allowed to react with diazomethane. The first of these was patterned after a procedure published by Gordon *et al.*[7] in a synthesis of **5** (using diazomethane) from **1**. In this experiment an ethereal solution of diazomethane was rapidly drawn, in small portions, through a filter funnel that contained 1-phenylurazole. Any unreacted diazomethane decomposes immediately on contact with acetic acid present in the filter flask. Thin-later chromatographic (TLC) data, by comparison with authentic samples, suggest that **5** and **6** are the sole monomethylated 1-phenylurazole analogues present in the reaction product. The TLC data are supported by the isolation of reaction products (see Experimental) and by results from ^{1}H NMR experiments which indicate that the monomethylated species **5** and **6** are the sole monomethylated 1-phenylurazoles formed.

The other investigation of the diazomethane–1-phenylurazole monomethylation regiochemistry was carried out using homogeneous reaction conditions. Unlike the reactions in protocol D (in which an excess of ethereal diazomethane was allowed to react with **1** dissolved in methanol), in this reaction *ca* 1 equiv. of ethereal diazomethane was added (in portions) to a methanolic solution of **1**. In addition to unreacted starting material (isolated in 76% yield), five products were isolated from this reaction: the monomethylated species **5** (9%) and **6** (5%), and the dimethylated species **2** (*ca* 1%), **3** (*ca* 1%) and **4** (6%). From a qualitative standpoint, the outcome of this experiment is therefore consistent with other experiments described in this paper and previously published work.

It remained for us to rationalize the absence of **7–9** as products for the reactions in which other monomethylated analogues of **1** were formed (i.e. **5** and **6**). There is substantial evidence for the hypothesis that the initial bond-making/bond-breaking reaction between diazomethane and a suitable 'electrophile' results in the transfer of a proton from the electrophile to diazomethane.[4]

While the reaction of diazomethane and the hydrazyl proton present in **1** results in the formation of **5** and **6**, reaction of diazomethane and the imide proton present in **1** would result in the formation of **7–9**. It therefore seems reasonable to attempt to rationalize the presence of **5** and **6**, and the absence of **7–9**, based on the thermodynamic acidities of the hydrazyl (#2N) and imide (#4N) protons present in **1**. In both DMSO and aqueous solution, the hydrazyl proton in 1-phenylurazole (**1**; $pK_a = 9{\cdot}9$[4b] in DMSO, $4{\cdot}8$[7] in H_2O) is more acidic than the imide proton in the same species

* A referee has pointed out that **5** and **8** are tautomers and are therefore difficult to separate and/or distinguish from one another. Evidence presented in this paper (TLC results, synthetic procedures, and comparisons of pK_a values) suggests that **5** and **6** are the sole monomethylaled intermediates formed when **1** is allowed to react with excess diazomethane. However, we cannot completely rule out the possibility that a small fraction of **8** exists in equilibrium with **5**.

($pK_a \approx 11{\cdot}1$* in DMSO, 7† in H_2O). It is likely that the aqueous acidity data provide a more accurate basis for comparison of the reactivities of the imide and hydrazyl protons for the homogeneous methanolic reactions carried out in protocols C and D. We believe that the $\geqslant 2$ pK_a unit difference in aqueous acidities between the hydrazyl and imide protons in **1** is more than sufficient to account for the presence of the monomethylated species **5** and **6** (and the absence of **7–9**) in these reactions.

Reaction pathway

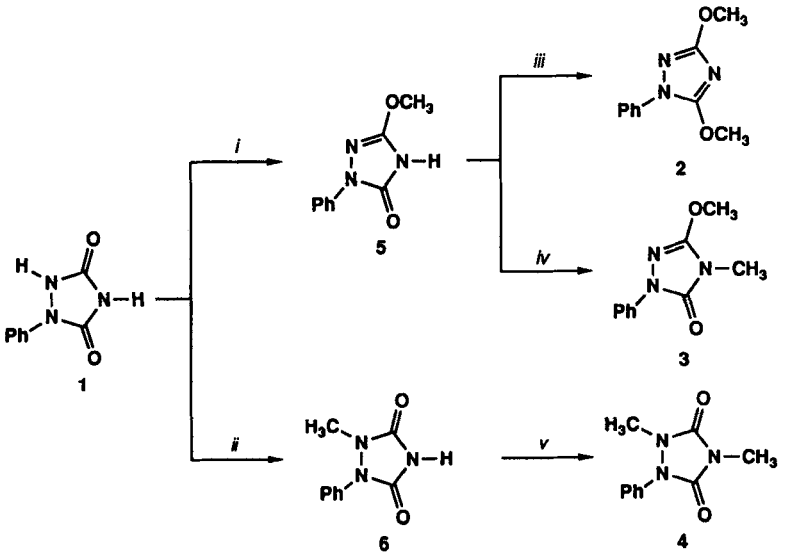
The results summarized in this paper suggest that **2–4** are the sole products when 1-phenylurazole (**1**) is allowed to react with excess diazomethane. Also described in this paper are experiments in which 1-phenylurazole was allowed to react with diazomethane in reactions that resulted in the formation of monomethylated 1-phenylurazole analogues **5** and **6**. A reaction pathway consistent with these results is shown in Scheme 1.

Owing to the heterogeneous nature of the reactions carried out using protocol A [in which a given urazole was added (in its solid state) to an excess of ethereal diazomethane] and also protocol B (in which an ethereal solution of diazomethane was added in portions to a suspension of ethereal 1-phenylurazole), neither protocol A nor B is particularly well suited to speculation regarding the pathway(s) responsible for the production of **2**, **3** and **4**. On the other hand, protocols C and D (in which ethereal solutions of diazomethane and methanolic solutions of 1-phenylurazole were allowed to react) do not suffer from the ambiguity that results from solution heterogeneity, since the medium is homogeneous throughout the entire course of both sets of reactions. We therefore propose the sequence of reactions shown in Scheme 1 to account for the products observed in the homogeneous reactions in which 1-phenylurazole was dissolved in methanol. Since **2**, **3** and **4** are isolated in significant amounts when using any of the four protocols (A, B, C and D), it is likely that the general features of the reaction sequence in Scheme 1 also apply to the heterogeneous reactions carried out in diethyl ether.

Evidence for our postulate that **5** and **6** are formed as the primary monomethylated intermediates in the diazomethane-induced dimethylation of **1** (steps i and ii in Scheme 1) was presented earlier. Steps iii-v in Scheme 1 are plausible in the light of related experiments. In results consistent with those described in this paper for the diazomethane-induced dimethylation of 1-phenylurazole (**1**), in our laboratory, when 1-phenyl-

* The DMSO pK_a of the imide proton in urazole has been estimated to be about 13.[4b] The experimentally derived DMSO pK_a for 1,2-dimethylurazole (12.25[4b]) therefore suggests that each hydrazyl CH_3 group acidifies the imide NH proton in urazole by 0·3–0·4 pK_a units. Since the pK_a of 1-phenyl-2-methylurazole is 10·8,[11] the estimated DMSO pK_a for the imide proton in 1-phenylurazole (**1**) is therefore *ca* 11·1–11·2.

† The aqueous pK_a for the imide proton in 1-phenylurazole (**1**) was estimated in the following way. In water, the pK_a values for hydantoin and 1-methylhydantoin are nearly equal (9·0 and 9·1, respectively[4b]). Since the aqueous pK_a for 1-phenyl-2-methylurazole is 6·97,[8] we estimate the aqueous pK_a for the imide proton in 1-phenylurazole is also *ca* 7.



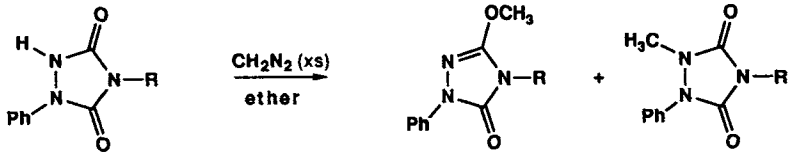
Scheme 1

3-methoxy-Δ^2-1,2,4- triazoline-5-one (**5**) was allowed to react with diazomethane (under various reaction conditions), **2** (as in step iii) and **3** (as in step iv) were formed in a ratio of *ca* 1:1·5–2·2. Step v, the conversion of 1-phenyl-2-methylurazole (**6**) into 1-phenyl-2,4-dimethylurazole (**4**), has been carried out previously, using diazomethane as the methylating agent.[3,5] We have duplicated these results; in our hands the reaction proceeds in quantitative yield. It therefore seems likely that **2**, **3** and **4** result from the sequence of reactions shown in Scheme 1.

Other urazoles

Finally, we summarize our investigations of the reactions of diazomethane and two other urazoles. As in the reactions between diazomethane and 1-phenylurazole, diazomethane-induced methylation of 1-phenyl-4-methylurazole (**7**) and 1,4-diphenylurazole (**10**) results in the formation of products different from those described previously.

In our hands, the diazomethane-induced methylations of **7** and **10** proceed as shown in equation (2). In



(2)

	Protocol	% Yield	% Yield	Total Yield
7: R=CH_3	A	46	52	97
	B	55	43	98
10: R=C_6H_5	A	52	46	98
	B	60	36	96

both cases, using both protocols A and B, substantial quantities of *N*- and *O*-alkylated products were isolated. An earlier report stated that **7** was methylated only on oxygen, whereas **10** was thought to undergo methylation only on nitrogen.[5] The chemistry depicted in equation (2) is consistent with other results described in this paper, and provide additional evidence for the ambient nature of 1-phenyl-4-substituted urazoles, when allowed to react with diazomethane.

CONCLUSION

In conclusion, we find that three products are formed (in greater than 90% overall yield) when 1-phenylurazole is allowed to react with diazomethane under conditions that result in its exhaustive methylation: 1-phenyl-3,5-dimethoxy-1,2,4-triazole (**2**), (the previously observed) 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one (**3**) and 1-phenyl-2,4-dimethylurazole (**4**). Compounds **2**–**4** are formed in substantial amounts regardless of the order of addition of the reagents, and regardless of whether 1-phenylurazole is present as a solid (in diethyl ether) or dissolved in methanol.

The nature of the monomethylated 1-phenylurazoles formed when **1** is allowed to react with diazomethane has been probed by allowing **1** to react with less than 2 equiv. of diazomethane. Whereas 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (**5**) and 1-phenyl-2-methylurazole (**6**) were shown to be formed in these reactions, 1-phenyl-4-methylurazole (**7**) and 1-phenyl-3-methoxy-Δ^3-1,2,4-triazolin-5-one (**8**) and 1-phenyl-5-methoxy-Δ^4-1,2,4-triazolin-3-one (**9**) were never observed. The relative thermodynamic protonic acidities of the imide and hydrazyl protons in 1-phenylurazole were cited as likely reasons for these observations. Based on these and other facts, a sequence of reactions has been proposed that accounts for the formation of the products (**2**–**4**) that result when **1** is allowed to react with excess diazomethane.

Diazomethane-induced methylations of 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (**5**), 1-phenyl-4-methylurazole (**7**) and 1,4-diphenylurazole (**10**) are similar in that *N*- and *O*-alkylated products are observed in these reactions also.

EXPERIMENTAL

Materials. The syntheses of 1-phenyl-4-methylurazole (**7**) and 1,4-diphenylurazole (**8**) were described previously.[4b] A Thomas–Hoover UniMelt melting point apparatus was utilized in the collection of the uncorrected melting point data.

Preparation of diazomethane. As described previously,[12] potassium hydroxide (20 ml; 40% aqueous solution) was added to diethyl ether (65 ml) and the mixture was cooled to 5 °C. With continuous

cooling and shaking, finely powdered nitrosomethylurea (6·5 g) was added in small portions. The deep yellow ether layer was then decanted and dried over magnesium sulfate. Solutions prepared in this way contain *ca* 1·8 g of diazomethane;[12] the diazomethane concentrations are *ca* 0·65 M. Ethereal diazomethane synthesized in this fashion was allowed to react with 1-phenylurazole and additional urazoles by the procedures below, including protocols A, B, C, and D.

1-Phenylurazole (**1**). A mixture of biuret (5·15 g, 50 mmol), phenylhydrazine (5·4 g, 50 mmol) and mineral spirits (40 ml) was heated at 160 °C in an oil-bath. After the ammonia was driven off, the mixture was cooled to room temperature and the solvent was poured off. The residue was then dissolved in aqueous ammonia, forming a light red solution. Filtration and treatment with concentrated HCl gave 1-phenylurazole (7·6 g, 86% yield); m.p. 259–260 °C (from EtOH; lit.[7] m.p. 268 °C).

Exhaustive methyalation of **1** *using diazomethane. Protocol A.* 1-Phenylurazole (1·70 g, 9·6 mmol) was added to ethereal diazomethane (60 ml, *ca* 39 mmol CH_2N_2). The reaction was monitored by TLC and by observing the evolution of nitrogen from the light yellow solution. The solution was allowed to stand for 1 h after cessation of the nitrogen evolution. The ether was then evaporated. Thin-layer chromatography indicated the presence of three different products. Separation via column chromatography [silica gel adsorbent and ethyl acetate–hexane (40 : 60) eluent] afforded three compounds. Isolated were 1-phenyl-3,5-dimethoxy-1,2,4-triazole [**2**, 0·48 g (24%); m.p. 43–44 °C (from pentane); ^{1}H NMR (DMSO-d_6) δ 7·767–7·28 (m, 5H, C_6H_5), 4·01 (s, 3H, OCH_3) 3·89 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6) δ 164·6, 157·5, 136·6, 129·7, 126·7, 120·7, 59·4, 56·4]; 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one [**3**, 0·66 g (34%); m.p. 95–96 °C (from hexane; lit.[7] m.p. 95 °C); ^{1}H NMR (DMSO-d_6), δ 7·88–7·15 (m, 5H, C_6H_5), 4·03 (s, 3H, OCH_3), 3·09 (s, 3H, NCH_3); ^{13}C NMR (DMSO-d_6), δ 152·0, 150·1, 138·0, 128·9, 124·0, 117·3, 56·4, 25·8]; and 1-phenyl-2,4-dimethylurazole [**4**, 0·75 g (38%); m.p. 94–95 °C (from ethyl acetate–pentane; lit.[7] m.p. 95 °C); ^{1}H NMR (DMSO-d_6), δ 7·54–7·31 (m, 5H, C_6H_5), 3·02 (s, 3H, NCH_3), 2·99 (s, 3H, NCH_3); ^{13}C NMR (DMSO-d_6), δ 155·6, 152·4, 135·5, 129·2, 126·6, 122·5, 33·9, 25·4]. Elemental analyses (Atlantic Microlab, Norcross, GA, USA) were performed for the isomeric species **2**, **3** and **4**. Calculated for $C_{10}H_{11}N_3O_2$ (i.e. **2**, **3** and **4**), C 58·52, H 5·40, N 20·48, found, for **2**, C 58·50, H 5·42, N 20·50%; for **3**, C 58·45, H 5·41, N 20·38%; for **4**, C 58·57, H 5·41, N 20·57%.

Protocol B. Ethereal diazomethane (*ca* 15 ml, 9·8 mmol CH_2N_2) was added in portions to a suspension of 1-phenylurazole (0·260 g, 1·47 mmol) in diethyl ether (100 ml). The solution was allowed to stand for 2 h. After removal of solvent, the residue was separated by column chromatography yielding **2** [0·075 g (25%)], **3** [0·100 g (33%)] and **4** [0·085 g (28%)].

Protocol C. 1-Phenylurazole (0·35 g, 2·0 mmol) was dissolved in methanol (100 ml). This solution was added to an ethereal solution of diazomethane (15–20 ml, *ca* 10–13 mmol CH_2N_2). The solution was allowed to stand for 2 h. After removal of solvent, the residue was separated by column chromatography yielding **2** [0·08 g (20%)], **3** [0·18 g (32%)] and **4** [0·19 g (46%)].

Protocol D. 1-Phenylurazole (0·104 g, 0·58 mmol) was dissolved in methanol (100 ml). To this, ethereal diazomethane (*ca* 5 ml, 3·2 mmol CH_2N_2) was added slowly. The solution was allowed to stand for 2 h. After removal of solvent, the residue was separated by column chromatography yielding **2** [0·017 g (18%)], **3** [0·042 g 35%)] and **4** [0·055 g (46%)].

Reaction of **1** *and ca 1 equiv. of diazomethane.* 1-Phenylurazole (0·89 g, 5·03 mmol) was dissolved in methanol (200 ml). To this solution, ethereal diazomethane (*ca* 8 ml, 5·1 mmol CH_2N_2) was added slowly, in portions. The solution was allowed to stand for 2 h. After removal of solvent, the resulting solid was extracted several times with hot $CHCl_3$. The substrate (i.e. 1-phenylurazole) was found to be insoluble in hot $CHCl_3$. Therefore, hot filtration of the $CHCl_3$ suspension was carried out; substantial unreacted 1-phenylurazole (0·68 g, 76%) was isolated in this fashion. TLC analyses of the combined $CHCl_3$ extracts indicated the presence of five products. The combined $CHCl_3$ extracts were concentrated to dryness. The solid residue was separated by column chromatography yielding **2** [*ca* 0·01 g (*ca.* 1%)], **3** [*ca* 0·01 g, (*ca* 1%)], **4** [0·06 g (6%)], **5** [0·09 g (9%)] and **6** [0·05 g (5%)]. The isolated yields for **2**–**6** suggest that some of the diazomethane decomposed prior to reaction with **1**.

Reaction of **1** *(present in a filter funnel) and diazomethane: synthesis of 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one* (**5**). Ethereal diazomethane (*ca* 120 ml, 78 mmol CH_2N_2) was drawn through a Buchner funnel that contained 1-phenylurazole (6·0 g, 34 mmol), into an aqueous solution of acetic acid (20 ml, 20%). The diethyl ether was evaporated off and the residue dissolved in EtOH (5 ml), and basified with dilute KOH. Water was added and the precipitated dimethyl derivatives were separated and a further amount removed by diethyl ether extraction. Acidification with dilute H_2SO_4 resulted in 1-phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (0·93 g, 4·9 mmol,

15% conversion) as white needles (from aqueous EtOH); m.p. 196–198 °C (lit.[7] m.p. 197 °C).

In an additional experiment carried out using the same protocol, the same reagents were allowed to react. In this case a smaller amount of 1-phenylurazole (3·0 g, 16 mmol) was employed. Treatment of the crude reaction product with dilute KOH (as described above) allowed the separation and isolation of a mixture of monomethylated derivatives (i.e. **5** + **6**, 0·86 g, 4·2 mmol, 26% conversion) from the dimethylated derivatives. Crystallization of the mixture of **5** and **6** (from aqueous EtOH) afforded pure **5** (0·40 g, 1·9 mmol, 12% conversion). The material that did not crystallize (0·46 g after evaporation of the aqueous EtOH) was shown, via ^{1}H NMR, to consist of a 1 : 1 mixture of **5** and **6**. No ^{1}H NMR signals other than those attributable to **5** and **6** were observed.

Reaction of 5 and excess diazomethane. Protocol A. 1-Phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (0·112 g, 0·586 mmol) was allowed to react with ethereal diazomethane (*ca* 4 ml, 2·6 mmol CH_2N_2). Separation of the products via column chromatography afforded 1-phenyl-3,5-dimethoxy-1,2,4-triazole [**2**, 0·035 g (29%)] and 1-phenyl-3-methoxy-4-methyl-$\Delta^2$2-1,2,4-triazoline-5-one [**3**, 0·080 g (66%)].

Protocol B. 1-Phenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one (0·087 g, 0·455 mmol) was allowed to react with ethereal diazomethane (*ca* 4 ml, 2·6 mmol CH_2N_2). Separation of the products via column chromatography afforded **2** [0·029 g (31%)] and **3** [0·064 g (68%)].

1-Phenyl-2-methylurazole (**6**). 1-Phenylurazole (1·77 g, 10 mmol) was dissolved in water (15 ml) which contained 1·0 equiv. of potassium hydroxide (0·64 g, 10 mmol). Ethanol (10 ml) was added to the mixture. After cooling in a water-bath, methyl iodide (1·77 g, 12·5 mmol) was added dropwise. The mixture was then stirred overnight. After removal of the solvents, hot ethyl acetate (3 × 15 ml) was added to extract the residue. The solution was filtered and ethyl acetate was evaporated, yielding 1-phenyl-2-methylurazole as a white crystalline solid, m.p. 183–184 °C (from EtOH; lit.[7] m.p. 183 °C).

Reaction of 6 and excess diazomethane. Protocol A. 1-Phenyl-2-methylurazole (0·200 g, 1·05 mmol) was allowed to react with ethereal diazomethane (*ca* 6 ml, 3·9 mmol CH_2N_2). After removal of the solvent, 1-phenyl-2,4-dimethylurazole [**4**, 0·214 g (99%)] was isolated.

Reactions of 1-phenyl-4-methylurazole (**7**) *and excess diazomethane. Protocol A.* 1-Phenyl-4-methylurazole (0·114 g, 0·596 mmol) was allowed to react with ethereal diazomethane (*ca* 4 ml, 2·6 mmol CH_2N_2). Separation of the products via column chromatography afforded 1-phenyl-3-methoxy-4-methyl-Δ^2-1,2,4-triazoline-5-one [**3**, 0·056 g (46%)] and 1-phenyl-2,4-dimethylurazole [**4**, 0·063 g (52%)].

Protocol B. 1-Phenyl-4-methylurazole (0·120 g, 0·628 mmol) was allowed to react with ethereal diazomethane (*ca* 4 ml, 2·6 mmol CH_2N_2). Separation of the products via column chromatography afforded **3** [0·071 g (55%)] and **4** [0·055 g (43%)].

Reactions of 1,4-diphenylurazole (**10**) *and excess diazomethane. Protocol A.* 1,4-Diphenylurazole (0·155 g, 0·607 mmol) was allowed to react with ethereal diazomethane (*ca* 5 ml, 3·2 mmol CH_2N_2). After removal of the solvent, separation of the products via column chromatography afforded 1,4-diphenyl-3-methoxy-Δ^2-1,2-4,triazoline-5-one [0·085 g (52%); m.p. 106–108 °C (from ethyl acetate–hexane); ^{1}H NMR (DMSO-d_6), δ 7·92–7·19 (m, 10H, C_6H_5), 4·04 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6), δ 150·8, 149·1, 137·8, 131·1, 129·1, 129·0, 128·5, 126·6, 124·4, 117·6, 56·6] and 1,4-diphenyl-2-methylurazole [0·074 g (46%); m.p. 130·5–132 °C (from ethyl acetate–hexane); ^{1}H NMR (DMSO-d_6), δ 7·65–7·35 (m, 10H, C_6H_5), 3·12 (s, 3H, NCH_3); ^{13}C NMR (DMSO-d_6), δ 154·0, 150·9, 135·2, 131·4, 129·2, 128·8, 128·2, 127·0, 126·5, 123·1, 33·9].

Protocol B. 1,4-Diphenylurazole (0·10 g, 0·39 mmol), suspended in diethyl ether (*ca* 70 ml), was allowed to react with ethereal diazomethane (*ca* 5 ml, 3·2 mmol CH_2N_2). Separation of the products via column chromatography afforded 1,4-diphenyl-3-methoxy-Δ^2-1,2,4-triazoline-5-one [0·063 g (60%)] and 1,4-diphenyl-2-methylurazole [0·037 g (36%)].

IR data. Infrared spectra were measured on a Perkin-Elmer Model 1420 ratio recording infrared spectrophotometer. All samples were prepared as 10% solutions in DMSO.

NMR data. A Variant VXR-300 MHz spectrometer was used to collect NMR data. In DMSO, the urazoles were present in concentrations of 0·1 M; TMS was used as the internal standard.

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