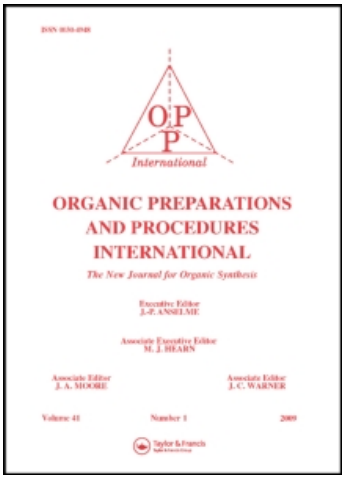


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

PREPARATION AND SOME SIMPLE REACTIONS OF 1-SUBSTITUTED IMIDAZOLE-2,4,5-TRIONES

Behzat Altural[a]; Yunus Akcamur[b]; Gert Kollenz[b]
[a] Science-Literature Faculty, Department of Chemistry, Erciyes University, Kayseri, Turkey [b] Institute of Organic Chemistry, Isotope Department, University of Graz, Graz, Austria

To cite this Article Altural, Behzat , Akcamur, Yunus and Kollenz, Gert(1991) 'PREPARATION AND SOME SIMPLE REACTIONS OF 1-SUBSTITUTED IMIDAZOLE-2,4,5-TRIONES', Organic Preparations and Procedures International, 23: 2, 147 — 151
To link to this Article: DOI: 10.1080/00304949109458301
URL: http://dx.doi.org/10.1080/00304949109458301

ORGANIC PREPARATIONS AND PROCEDURES INT., 23 (2), 147-151 (1991)

PREPARATION AND SOME SIMPLE REACTIONS OF 1-SUBSTITUTED IMIDAZOLE-2,4,5-TRIONES§

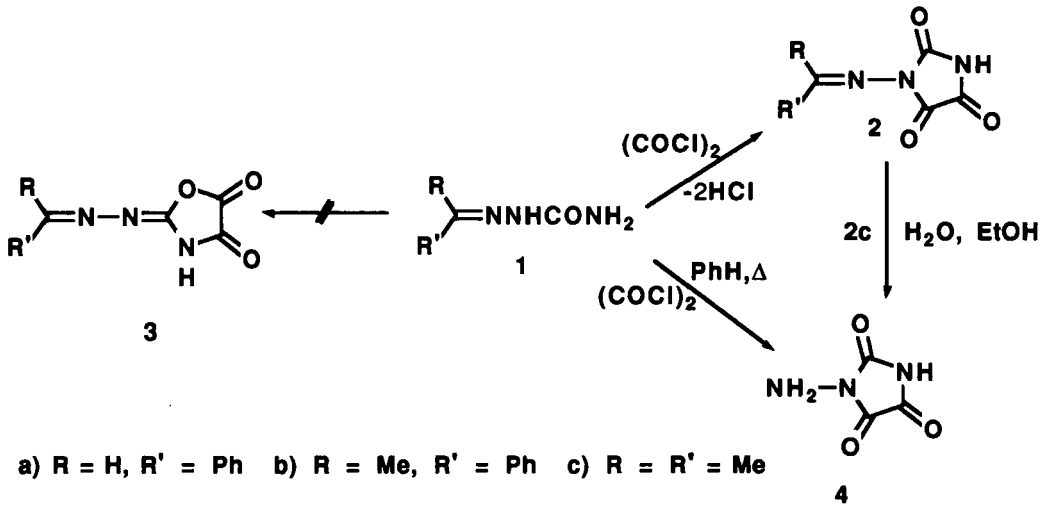
Behzat Altural†, Yunus Akcamur† and Gert Kollenz*††

† Science-Literature Faculty, Department of Chemistry
Erciyes University, TR-38039 Kayseri, TURKEY

†† Institute of Organic Chemistry, Isotope Department
University of Graz, A-8010 Graz, AUSTRIA

Oxalic acid and its derivatives, e.g. oxalyl chloride, are well known to be suitable C_2-building blocks in the synthesis of several heterocyclic systems.[1] In particular cyclocondensation reactions of substituted ureas and oxalyl chloride easily afford parabanic acid derivatives.[2] Surprisingly, to our knowledge only one parabanic acid derived from semicarbazones and oxalyl chloride has been described so far.[3] We report new examples following the known procedure[3] and subsequent reactions.

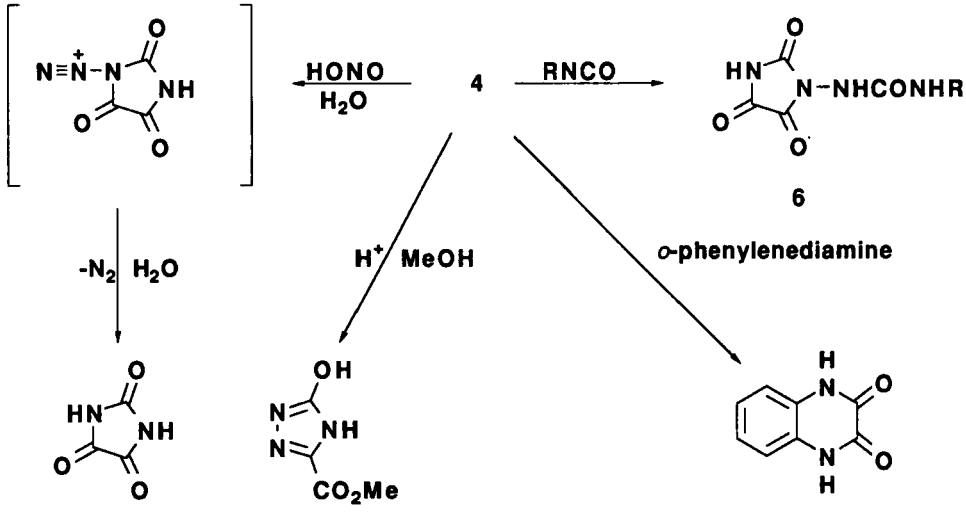
The semicarbazones **1** and oxalyl chloride cyclize to give the corresponding imidazoletriones **2** in 40-80% yield. From the characteristic strong IR absorption bands at



1730-1760 cm^{-1}, the presence of a parabanic acid skeleton instead of an isomeric oxazoletrione moiety (**3**) can easily be deduced, since the latter show characteristic IR absorptions somewhat above 1800 cm^{-1}.[4,5] As an example, **2c** is rapidly hydrolyzed by

heating in ethanolic solution for 3-5 minutes to give the corresponding 1-aminoparabanic acid **4**, which on the other hand is also obtained in rather low yields (30-40%) starting with the semicarbazones **1b,c** and oxalyl chloride in boiling benzene. Obviously hydrolysis of the C=N double bond must have occurred during that reaction since semicarbazide itself cannot be cyclized to **4** by use of oxalyl chloride. Compound **4** exhibits the carbonyl absorption bands of the parabanic acid moiety at 1760 cm^{-1} and the corresponding signals in the C-13 NMR spectrum at 154.8 (C-2), 157.8 and 158.6 ppm (C-4,C-5 or vice versa) respectively.

It is interesting to note that **4** has been proposed as an intermediate in the conversion of **2a** to the 1,2,4-triazole-3-carboxylic acid methyl ester **5**.[6] This could now be established by starting the methanolysis with **4** instead of **2a** which again - as expected - led to the triazole derivative **5** thus confirming the former mechanistic proposal.[6] Furthermore the N-NH_2 moiety in **4** should be capable of several subsequent reactions: **4** adds to arylisocyanates yielding the corresponding imidazolylureas **6**. This behavior in general is well known from heterocumulene chemistry[7] and was also observed with several cyclic N-NH_2 compounds similar to **4**.[4c,7c] Attempts to again cyclize the urea side-chain in **6** with oxalyl chloride to obtain bis-parabanic acid derivatives failed. Quinoxaline-2,3-dione (**8**)[8] is obtained from reaction of **4** and o-phenylenediamine. The attack of the amine may open the imidazoletrione ring leading to an exchange of the semicarbazide moiety against the stronger nucleophilic diamine.



a) R = C_6H_5 b) R = 4-MeC_6H_4 c) R = 1-$C_{10}H_7$

Attempts to eventually get a fairly stable diazonium salt from diazotization reaction of **4** failed since parabanic acid is isolable as the stable end product. This should be the result of a deamination process via an initially formed diazonium salt intermediate and subsequent

elimination of nitrogen, which agrees well with earlier results reported with compounds possessing similar N-NH_2 structural features.[4c,9] Nevertheless it is worthwhile to note that a reductive process seems to be essential to explain these transformations of N-NH_2 into NH groups.

EXPERIMENTAL SECTION

Melting points are uncorrected. The IR spectra were recorded on a Perkin-Elmer 421 spectrometer using samples in potassium bromide disks. The ^{13}C NMR spectrum of **4** ($CDCl_3$) was determined on a Varian XL 200 spectrometer. The elemental analyses were obtained from a Carlo Erba Elemental Analyzer.

1-(Phenylmethyleneamino)imidazole-2,4,5-(1H,3H)-trione (**2a**)[3].- A mixture of 300 mg (1.84 mmole) **1a** and 0.16 ml (1.84 mmole) of oxalyl chloride in 10 ml of benzene was kept at 50-60° for 1.5 hr. After cooling the precipitate was collected yielding 240 mg (60%) of **2a** as colorless needles, mp. 205° (acetic acid). The mp, IR spectrum and Rf value of **2a** were identical with those of an authentic sample, prepared following ref. 3. IR (KBr): 3240 (broad, NH), 1820 w, 1730 s (CO) cm^{-1}.

1-(Methylphenylmethyleneamino)imidazole-2,4,5-(1H,3H)-trione (**2b**).- A mixture of 100 mg (0.56 mmole) of **1b** and 0.06 ml (0.67 mmole) of oxalyl chloride was stirred in 5 ml of anhydrous ether at 20° for 3 hrs. The colorless precipitate was washed with anhydrous ether and crystallized from dry ethanol to give 120 mg (85%) of **2b**, mp. 187-188°. IR (KBr): 3040 (broad, NH), 1820 w, 1780 w, 1750 s (CO) cm^{-1}.

Anal. Calcd. for $C_{11}H_9N_3O_3$: C, 57.14; H, 3.89; N, 18.18
Found: C, 57.09; H, 3.88; N, 18.15

1-(Dimethyleneamino)imidazole-2,4,5-(1H,3H)-trione (**2c**). - To a well stirred suspension of 250 mg (2.1 mmoles) of **1c** in 10 ml of anhydrous ether, 0.225 ml (2.6 mmoles) of oxalyl chloride was added dropwise at 20° during 30 min and the mixture was kept stirring for 4 hrs. Then the crude product was collected and washed with anhydrous ether to yield 220 mg (60%) of colorless **2c**, mp. 184-185° (without recrystallization). IR (KBr): 3040 (broad, NH), 1840 w, 1760 s (CO) cm-1 .

Anal. Calcd. for $C_6H_7N_3O_3$: C, 42.60; H, 4.14; N, 24.85
Found: C, 42.40; H, 4.24; N, 24.97

1-Aminoimidazole-2,4,5-(1H,3H)-trione (**4**). - (a) **2c** (100mg, 0.6 mmole), dissolved in 2 ml ethanol (96%), was refluxed for 3-5 min. After cooling, 50 mg (61%) of **4**, mp. 185° (ethanol) was obtained. IR (KBr): 3350, 3180 (NH, NH_2), 1790, 1740 s (CO) cm^{-1}. ^{13}C-NMR spectrum ($CDCl_3$), see discussion above.

Anal. Calcd. for $C_3H_3N_3O_3$: C, 27.90; H, 2.32; N, 32.55
Found: C, 27.77; H, 2.45; N, 32.27

(b) A mixture of 2g (11.3 mmole) of **1b** and 1 ml (11.4 mmoles) of oxalyl chloride in 20 ml of benzene was refluxed with stirring for 4 hrs. After cooling, the colorless precipitate (520

mg, 36%) was shown to be **4**, from mp, TLC and IR spectrum.

(c) Following the procedure given in (b), from 1g (8.7 mmoles) of **1c** and 0.75 ml (8.8 mmoles) of oxalyl chloride in 10 ml of benzene, 390 mg (35%) **4** was isolated.

Synthesis of Compounds **6**. General Procedure.- A mixture of **4** and of the corresponding arylisocyanate (20% excess) was refluxed in acetonitrile for 3-6 hrs and stirred at 20° for additional 12 hrs. Then the colorless precipitate was collected, extensively washed with anhydrous ether and recrystallized from a suitable solvent (acetic acid or ethanol).

1-(Imidazole-2,4,5-trioxoperhydro-1-yl)-3-phenylurea (**6a**). - **4** (100 mg) and phenylisocyanate, after 6 hrs, afforded 80 mg (42%) of **6a** , mp. 226-227° (acetic acid). IR (KBr): 3260 (NH), 1780 w, 1760 s (CO) cm^{-1}.

Anal. Calcd. for $C_{10}H_8N_4O_4$: C, 48.38; H, 3.22; N, 22.58
Found: C, 48.27; H, 3.31; N, 22.49

1-(Imidazole-2,4,5-trioxoperhydro-1-yl)-3-p-tolylurea (**6b**). - **6b** (190 mg, 46%), mp. 232-234° (ethanol) was obtained from 100 mg of **4** after 5 hrs. IR (KBr): 3260 (NH), 1780 w,1760 s (CO) cm^{-1}.

Anal. Calcd. for $C_{11}H_{10}N_4O_4$: C, 50.38; H, 3.82; N, 21.37
Found: C, 50.65; H, 3.90; N, 21.47

1-(Imidazole-2,4,5-trioxoperhydro-1-yl)-3-(1-naphthyl)urea (**6c**). - A mixture of 250 mg (1.95 mmole) of **4** and of **5c** reacted for 3 hrs to yield 200 mg (34%) of **6c** , mp. 223-224° (ethanol). IR (KBr): 3280 (NH), 1800 w, 1750 s (CO) cm^{-1}.

Anal. Calcd. for $C_{14}H_{10}N_4O_4$: C, 56.37; H, 3.35; N, 18.79
Found: C, 56.22; H, 3.40; N, 18.81

Methyl 5-Hydroxy-1,2,4-triazole-3-carboxylate (**5**)[6].- To a suspension of 100 mg (0.77 mmole) of **4** in 2 ml of methanol 0.17 ml HCl conc. was added. The mixture was refluxed for 6 hrs and after cooling the colorless precipitate was recrystallized from water to give 80 mg (72%) of **5** identified by mp and spectroscopic data according to the literature.[6]

Imidazole-2,4,5-(1H,3H)-trione ("Parabanic acid") (**7**)[2a,b]. - One ml of water and 0.15 ml HCl conc. were added to a suspension of 100 mg (0.77 mmole) of **4** and 106 mg (1.54 mmole) of $NaNO_2$ and the mixture was stirred for 10 min at 20°. After evaporation to dryness, the residue was crystallized from ethanol to afford 60 mg (68%) of **7** which was identical with an authentic sample of parabanic acid by mp, TLC and IR spectrum.

Quinoxaline-2,3-(1H,3H)-dione (**8**)[8]. - A mixture of 200 mg (1.55 mmole) of **4** and of 167 mg (1.55 mmole) of o-phenylenediamine was refluxed for 20 min in 15 ml of ethanol. Upon cooling, 60 mg (24%) of **8** was obtained, identical by mp, IR spectrum and TLC, with an authentic sample.[8]

REFERENCES

§ Reactions of Cyclic Oxalyl Compounds, XXXI

1. Recent Review : R. Beckert and R. Mayer, Wiss. Z. Techn. Univ. Dresden, 36, 87 (1987); Chem. Abstr., 108, 167337a (1988).

2. (a) H. Biltz and E. Topp, Ber., 46, 1387 (1913); (b) J. E. Franz and C. Osuch, J. Org. Chem., 29, 2592 (1964); (c) L. M. Myl'nikova, Y. A. Mandelbaum and R. S. Soifer, Z. Obsch. Chim., 50, 1319 (1980); (d) R. Richter, B. Tucker and H. Ulrich, J. Org. Chem., 43, 4150 (1978); (e) W. Ried, W. G. Broft and J. W. Bats, Chem. Ber., 116, 1547 (1983).

3. R. L. White and T. L. Schwan, J. Pharm. Sci., 65, 135 (1976).

4. (a) H. Ulrich and A. A. R. Saying, Angew. Chem. Int. Ed. Engl., 5, 704 (1966); (b) J. Org. Chem., 30, 2781 (1965); (c) B. Altural and G. Kollenz, Monatsh. Chem., 121, 677 (1990).

5. (a) J. C. Sheehan and E. J. Corey, J. Am. Chem. Soc., 74, 360 (1952); (b) A. J. Speciale and L. R. Smith, J. Org. Chem., 28, 1805 (1963); (c) T. Sasaki, S. Eguchi and T. Toru, Tetrahedron Lett., 4135 (1968).

6. T. J. Schwan and R. L. White, J. Heterocyclic Chem., 12, 771 (1975).

7. (a) J. H. Saunders and R. J. Slocombe, Chem. Rev., 43, 203 (1948); (b) R. G. Arnold, J. A. Nelson and J. J. Verbanc, ibid., 57, 47 (1957); (c) M. J. Hearn and L. Lucas, J. Heterocyclic Chem., 21, 615 (1984).

8. (a) O. Aschan, Ber., 18, 299 (1885); (b) O. Hinsberg, ibid., 41, 2032 (1908).

9. (a) T. Curtius, A. Darapsky and E. Müller, ibid., 40, 815 (1907); (b) H. Beyer and G. Walter, Chem. Ber., 89, 1657 (1956); (c) Y. A. Ibrahim, M. M. Eid and S. A. Abdel Hady, J. Heterocyclic Chem., 17, 1733 (1980).

(Received March 20, 1990; in revised form October 10, 1990)