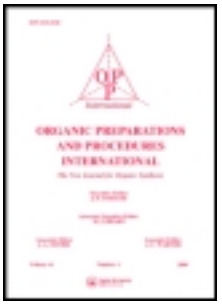


Organic Preparations and Procedures International: The New Journal for Organic Synthesis

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uopp20

NEW SYNTHESIS OF PHENYLTHIOGLYCOLIC ACIDS via RELATED TRIAZENE COMPOUNDS

Ali Disli [a] & Yilmaz Yildirir [a]

[a] Department of Chemistry Faculty of Arts and Sciences , Gazi University , 06500, Teknikokullar, Ankara, TURKEY

Published online: 09 Feb 2009.

To cite this article: Ali Disli & Yilmaz Yildirir (1998) NEW SYNTHESIS OF PHENYLTHIOGLYCOLIC ACIDS via RELATED TRIAZENE COMPOUNDS, Organic Preparations and Procedures International: The New Journal for Organic Synthesis, 30:3, 349-352, DOI: 10.1080/00304949809355295

To link to this article: http://dx.doi.org/10.1080/00304949809355295

ORGANIC PREPARATIONS AND PROCEDURES INT., 30 (2), 349-372 (1998)

OPPI BRIEFS

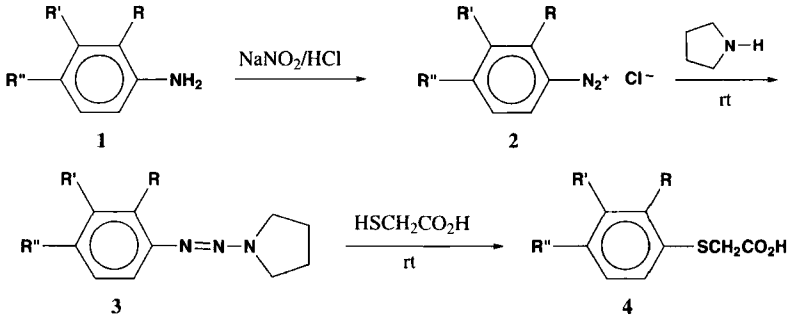
NEW SYNTHESIS OF PHENYLTHIOGLYCOLIC ACIDS *via* RELATED TRIAZENE COMPOUNDS

Submitted by (10/27/97)

Ali Disli and Yilmaz Yildirir*

Department of Chemistry
Faculty of Arts and Sciences
Gazi University
06500, Teknikokullar, Ankara, TURKEY

Substituted thioindoxyls are extensively used for the synthesis of vat dyestuff.[1,2] Of the many methods for their synthesis,[1,3] the most widely used is the cyclization of the appropriate arylthioglycolic acids.[4,5] We previously reported a more efficient two-step procedure for the synthesis of phenylthioglycolic acids[6,7] and also now describe a new procedure for the synthesis of these acids in yields higher than previously reported.



a) R = F, R', R" = H b) R, R' = H, R" = F c) R = Cl, R', R" = H d) R, R' = H, R" = Cl
e) R = Br, R', R" = H f) R, R' = H, R" = Br g) R = I, R', R" = H h) R, R' = H, R" = I
i) R, R" = H, R' = NO_2 j)R, R' = H, R" = NO_2 k) R, R' = H, R" = CH_3 l) R = COOH, R', R" = H

Aryltriazenes[8] are generally crystalline compounds which are stable to air, light, and basic conditions[9] and have been used for the synthesis of aryl iodides by replacement of the triazene moiety with iodine.[10,11] Although eleven thioglycolic acids could be synthesized by this method, the preparation of carboxyphenylthioglycolic acid from [2-carboxyphenyl)azo]pyrrolidine failed in this study. The product of this reaction was salicylic acid, possibly generated via the lactone as suggested in our previous paper.[7]

EXPERIMENTAL SECTION

The substituted anilines were supplied by Merck Co. All mps were determined in sealed capillaries. FT-IR spectra were recorded on a Matson 1000 spectrometer. ^{1}H NMR spectra were obtained on a Varian EM-360 L (60 MHz) NMR spectrometer. Elemental analyses were carried out on a Leco-CHN 600 instrument.

Typical Procedures. 2-Fluorophenylthioglycolic Acid.- A mixture of 2-fluoroaniline (5.55g , 0.05 mole) and 13.5 mL of conc. HCl was cooled about to -10°; then about 20 g of crushed ice was added and the mixture was diazotized by the slow addition of a solution of sodium nitrite (4.49 g, 0.065 mole) in 10 mL of water. The cold solution of diazotized amine (CAUTION!) was then added cautiously and slowly to a stirred solution of pyrrolidine (4.2 mL, 0.05 mole) and allowed to warm up to room temperature to give a precipitate, [(2-fluorophenyl)azo]pyrrolidine (**3a**) which was collected and dried in air (7.2 g, 75% yield). **CAUTION:** These compounds which bear the triazene moiety as part of their structure must be regarded as potentially carcinogenic and appropriate precautions taken to ensure that human contact does not occur.[8]

Thioglycolic acid (2.1 mL, 0.03 mole) was poured onto the finely powdered [(2-fluorophenyl)-azo]pyrrolidine (5.8g, 0.03 mole) at room temperature and mixed well. Then, 2.6 mL of conc. HCl (0.03 mole) was added to the mixture. The reaction was complete in several minutes after addition of hydrochloric acid. In order to extract thioglycollic acid from oily product, the reaction mixture was boiled in water and filtered, then allowed to cool. More of product (**4a**) crystallized from

TABLE 1. Yields, mps, IR and ^{1}H NMR Spectral Data of Compounds **3**

Cmpd	mp. (°C)	lit mp. (°C)	Yield (%)	IR (KBr) (pyrr. C-H) (cm^{-1})	^{1}H NMR (δ, CCl_4)
3a	37-38	—	75	2866,2979	1.9 (m, 4H); 3.72 (m,4H), 6.85-7.6 (m, 4H)
3b	57	—	71	2875,2975	1.8 (m, 4H); 3.6 (m,4H), 6.72-7.39 (m, 4H)
3c	53-55	—	64	2857,2953	1.9 (m, 4H); 3.7 (m,4H), 6.72-7.42 (m, 4H)
3d	59-60	—	61	2862,2982	1.9 (m, 4H); 3.67 (m,4H), 7.17 (s, 4H)
3e	54-55	54.5-55.5[a]	65	2864,2970	2.0 (m, 4H); 3.87 (m,4H), 6.9-7.73 (m, 4H)
3f	80-81	82-84[a]	90	2866,2960	2.0 (m, 4H); 3.73 (m,4H), 7.3 (s, 4H)
3g	55-57	—	60	2870,2955	2.08 (m, 4H); 3.8 (m,4H); 7.1 (d,2H); 7.56 (d, 2H)
3h	81-83	—	93	2870,2972	2.0(m, 4H); 3.7(m,4H), 7.25-8.18 (m, 4H)
3i	93-95	—	84	2873,2978	2.05 (m, 4H); 3.75(m,4H), 7.3-8.26 (m, 4H)
3j	78-80	—	93	2875,2976	2.05 (m, 4H); 3.75(m,4H), 7.3-8.26 (m, 4H)
3k	77	—	70	2880,2973	2.0 (m, 4H); 2.32 (s,3H); 3.77(m,4H), 6.9-7.35 (m, 4H)
3l	122-123	123-125[a]	87	2859,2973	1.45 (m,2H); 2.3 (m, 2H); 4.0 (m,4H), 7.3 (m, 4H)

a) Ref. 8

TABLE 2. Yields, mps, IR and ^{1}H NMR Spectral Data of Compounds **4**

Cmpd	mp. (°C)	lit mp. (°C)	Yield (%)	IR (KBr) (pyrr. C-H) (cm^{-1})	^{1}H NMR (δ, CCl_4)
4a	77-79	79[b]	37	1696	3.70 (s ,2H); 6.95-7.68 (m, 4H), 8.25 (broad, 1H)
4b	—	—	43[c]	1695	3.48 (s, 2H); 6.91 (d, 2H); 7,28 (d, 2H); 8.3 (s, 1H)
4c	117-118	117-118[d,e]	32	1705	3.68 (s, 2H); 7.29(m, 4H), 9.2 (broad, 1H)
4d	101-103	—	36	1702	3.50 (s, 2H); 7.21 (s, 4H), 10.19 (broad, 1H)
4e	115-116	116-117[f]	44	1705	3.78 (s, 2H); 7.1-7.79(m, 4H),10.3 (broad, 1H)
4f	105-107	107[g]	33	1702	3.73 (s, 2H); 7.5 (s, 4H), 8. 5 (broad, 1H)
4g	112-114	112-113[h]	38	1705	3.61 (s, 2H); 7.18-7.95 (d-d, 4H), 9.74 (broad, 1H)
4h	106-110	—	32	1702	3.68 (s, 2H); 7.2 (d, 2H);7.72 (d, 2H), 8.12(broad,1H)
4i	131-132	130-132[i]	37	1709	3.93 (s, 2H); 7.52-8.52 (m, 4H), 9.12 (broad, 1H)
4j	124-128	—	35	1707	3.76 (s, 2H); 7.35-8.35 (m, 4H), 9.08 (broad, 1H)
4k	96-97	95-97[i]	45	1704	2.34 (s, 3H); 3.64 (s, 2H); 7.05-7.50 (d-d, 4H), 8.6 (broad, 1H)

a) From anilines; b) N. Sharghi and I. Lalezari, *J. Chem. Eng. Data,* **8**, 276 (1963); c) Compound **4b** is a known product,[b] but could not be crystallized and was isolated a thick oil in 43% yield; d) Ref. 5; e) Ref. 6; f) G. M. Oksengendler and Yu. E. Gerasimenko, *J. Gen. Chem. USSR,* **29**, 919 (1959); g) P. Friedlander and A Chwaia,. *Monatsh. Chem.,* 247 (**1907**); h) N.S. Dokunikhin and Y. Gerasimenko, *Gen. Chem., USSR,* **30**, 1987 (1960); **i)** Ref. 7

the aqueous solution. The oily residue was boiled again in about 100 mL of water and filtered. This process was repeated more times and the solid crops were combined and recrystallized from water to yield 2.74 g (49%, 37% based to 2-fluoroaniline) of product, mp. 77-79°.

TABLE 3. Elemental Analyses of New Compounds **3a-3d**, **3g-3k** and **4d, h, j**

Cmpd	C (Found)	H (Found)	N (Found)
3a	62.16(62.19)	6.26(6.25)	21.75(21.75)
3b	62.16(62.14)	6.26(6.23)	21.75(21.77)
3c	57.28(57.29)	5.77(5.80)	20.04(20.00)
3d	57.28(57.31)	5.77(5.81)	20.04(20.01)
3g	39.89(39.91)	4.02(3.99)	13.95(13.98)
3h	39.89(39.87)	4.02(3.99)	13.95(13.93)
3″	54.54(54.57)	5.49(5.51)	25.44(25.48)
3j	54.54(54.51)	5.49(5.47)	25.44(25.43)
3k	69.81(69.84)	7.99(7.97)	21.67(21.65)
4d	74.41(74.43)	3.48(3.46)	—
4h	32.67(32.67)	2.40(2.42)	—
4j	45.06(45.03)	3.31(3.34)	—

REFERENCES

1. H. A. Lubs and A. L. Fox, *US Patent* **1936**, 2,061,200; *Chem. Abs.*, **31**, 881 (1937).
2. W. Carpmael, *Brit. Patent*, **1926,** 274,527; *Chem. Abs.*, **22**, 2277 (1928).
3. L. K. A. Rahman and R. M. Scrowston, *J. Chem. Soc., Perkin Trans. 1*, 385 (**1984**).
4. O. Dann and M. Kokurudz, *Chem. Ber.*, **86**, 1949 (1953).
5. C. E. Dalgliesh and F. G. Mann, *J. Chem. Soc.*, 893 (**1945**).
6. Y. Yildirir and G. Okay, *Org. Prep. Proced. Int.*, **23**, 198 (1991).
7. Y. Yildirir and A. Disli, *ibid.*, **27**, 381 (1995).
8. L. M. Gross, D. H. Blank and W. M. Welch, *J. Org. Chem.*, **58**, 2104 (1993).
9. E. B. Merkushev, *Synthesis*, 923 (**1988**).
10. Z. Wu, and J. S. Moore, *Tetrahedron Lett.*, **35**, 5539 (1994).
11. J. S. Moore, E. J. Weinstein, Z. Wu, *ibid.*, **32**, 2465 (1991).

****

A SIMPLE REGIOSELECTIVE SYNTHESIS OF (R)-10-HYDROXYAPORPHINE DIRECTLY FROM (R)-10,11-DIHYDROXYAPORPHINE [(R)-APOMORPHINE]

Submitted by (04/28/97)

Jack C. Kim*, Sang-Duk Bae, Ji-A Kim and Soon-Kyu Choi†

Department of Chemistry, Pusan National University
Pusan 609-735, Republic of KOREA

† *Department of Chemistry, Dong-A University*
Pusan 604-714, Republic of KOREA

Since the discovery of useful dopamine (DA) agonist activity in hydroxylated aporphine alkaloids such as (R)-apomorphine [(R)-10,11-dihydroxyaporphine] (**1**),[1] there has been continuing interest in delineating the portions of the apomorphine molecular structure responsible for dopaminergic properties and the structure-activity relationships of this class of conformationally rigid DA