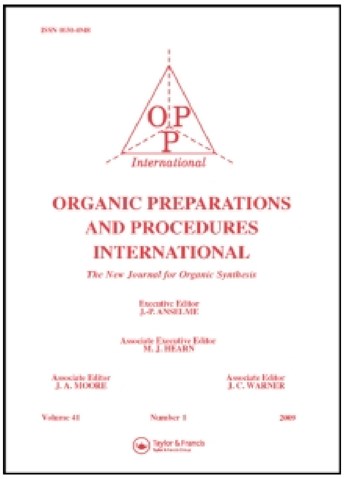
This article was downloaded by:
On: *27 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

REDUCTION OF 3- AND/OR 5-UNSUBSTITUTED 2-ETHYLPYRAZOLIUM SALTS WITH COMPLEX METAL HYDRIDES. SYNTHESIS OF PYRAZOLIDINES

Luis A. Bañuelos[a]; Purificaciön Cuadrado[a]; Ana M. González[a]; Francisco J. Pulido[a]
[a] Depanumento de Química Orgánica, Universidad de Vulladolid, Valladolid, Spain

To cite this Article Bañuelos, Luis A. , Cuadrado, Purificaciön , González, Ana M. and Pulido, Francisco J.(1992) 'REDUCTION OF 3- AND/OR 5-UNSUBSTITUTED 2-ETHYLPYRAZOLIUM SALTS WITH COMPLEX METAL HYDRIDES. SYNTHESIS OF PYRAZOLIDINES', Organic Preparations and Procedures International, 24: 2, 181 — 185

To link to this Article: DOI: 10.1080/00304949209355694

URL: http://dx.doi.org/10.1080/00304949209355694

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

the refluxing period. The hot slurry was filtered to afford 184 g of white solid containing 97% ether and 3% **3** by liquid chromatography. The solid was further purified by slurring in 800 mLof acetone and 200 ml of water and refluxing for one-half hour. Hot filtration of the slurry produced **11** of 98⁺% purity with a mp. 240-241°. ^{1}H NMR (DMSO-d_6): δ 2.26 (s, 12H), 4.75 (s, 4H), 7.50 (s, 2H).
Anal. Calcd. for $C_{18}H_{18}Br_4O_3$: C, 35.88; H, 2.99; Br, 53.16. Found: C, 35.96; H, 3.01; Br, 53.03

REFERENCES

1. M. M. Khan and H. Fatemi, *Proc. Int. Symp. Microel.*, 420 (1986); S. Ahmad, R. Blish, and T. Corbett, *Comp. Hybr. Manuf Technol.*, **9**, 379 (1986); R. J. Gale, *Proc. IEEE Int. Rel. Phys. Symp.*, 37 (1984); K. N. Ritz., W. T. Stacey and E. K. Broadbent, *ibid.*, 28 (1987); M. M. Khan, H. Faterrii, J. Romero, and E. Delenia, *ibid.*, 40 (1988).

2. C. S. Wang, D. B. Fritz and A. Mendoza, *ACS Symposium Series*, **407**, 397 (1988); D. B. Fritz and C. S. Wang, *ibid.*, **407**, 405 (1988); C. S. Wang, J. R. Berman, L. L. Walker and A. Mendoza, *J. Appl. Polym. Sci.*, 43,1315 (1991).

3. K. Auwers and H. Allendorf, *Ann*, **302**, 76 (1898).

4. A. Mendoza, *U. S. Patent* 4684752 (1988); C.A. **109**: 13549 (1988).

5. C. S. Wang and A. Mendoza, *Polym. Bulletin*, **25**, 279 (1991).

Downloaded At: 09:41 27 January 2011

****

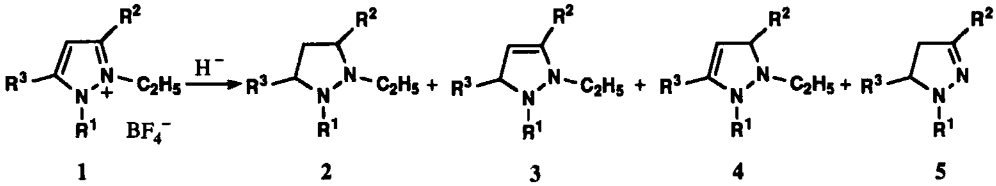
REDUCTION OF 3- AND/OR 5-UNSUBSTITUTED 2-ETHYLPYRAZOLIUM SALTS WITH COMPLEX METAL HYDRIDES. SYNTHESIS OF PYRAZOLIDINES

Submitted by (04/13/89)
Luis A. Bañuelos, Purificación Cuadrado,
Ana M. González* and Francisco J. Pulido

Departamento de Química Orgánica
Universidad de Valladolid
47011 Valladolid, SPAIN

Previous disclosures[1] described the regioselective synthesis of 3-pyrazolines by reduction of 1,3,5-trisubstituted 2-alkylpyrazolium salts with complex metal hydrides (CMH). The present investigation reports that the reduction of 3- and/or 5-unsubstituted 2-ethylpyrazolium salts with the same hydrides leads to results different from the above, giving pyrazolidines (**2**) as major products (Table 1).

The formation of pyrazolidines which does not depend of the molar ratio of hydride used,

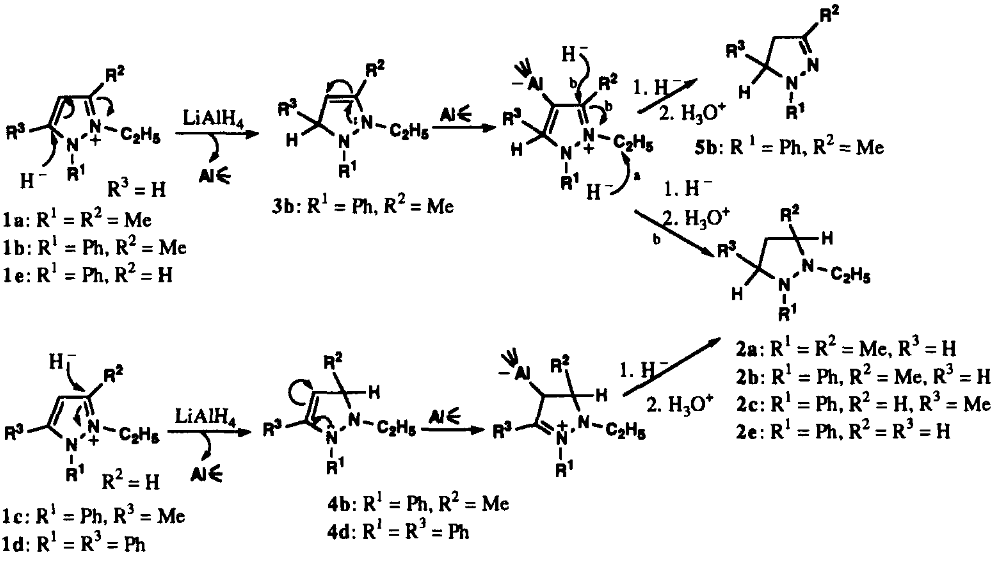


may be due to the low steric requirements of the 3- or 5-unsubstituted pyrazolium salts which are

TABLE 1 Reduction of 2-Ethylpyrazolium Tetrafluoroborates (1) with Complex Metal Hydrides[a]

Substrate No.	R^1	R^2	R^3	Hydride[f]	Solvent	Time (hrs)	Products and Yield (%)[b]
1a	Me	Me	H	$NaBH_4$[c]	EtOH	6	**2a** (79)
				$LiAlH_4$[c]	Et_2O	4	**2a** (55)[d]
1b	Ph	Me	H	$NaBH_4$[c]	EtOH	6	**2b** (80)
				$LiAlH_4$[e]	Et_2O	4	**3b** (50) + **4b** (31)
				$LTBH_4$[e]	THF	6	**4b** (45) + **5b** (24)
1c	Ph	H	Me	$NaBH_4$[e]	EtOH	6	**2c** (75)
				$LiAlH_4$[c]	Et_2O	4	**2c** (71)
				$LiAlH_4$[c]	THF	4	**2c** (60)
				$LTBH_4$[c]	THF	6	**2c** (67)
1d	Ph	H	Ph	$NaBH_4$[c]	EtOH	6	**4d** (75)
				$LiAlH_4$[c]	Et_2O	4	**4d** (80)
1e	Ph	H	H	$NaBH_4$[c]	EtOH	6	**2e** (82)
				$LiAlH_4$[c]	Et_2O	4	**2e** (77)
				$LTBH_4$[c]	THF	6	**2e** (73)

a) Reactions were carried out at room temperature. b) Yields refer to isolated pure products. c) Molar ratio 1:hydride = 1:2. d) Isolated as a complex with borane. e) Molar ratio 1:hydride =1:1. f) LTBH = LiAl (O-Bu-*t*)$_3$H.



Downloaded At: 09:41 27 January 2011

Downloaded At: 09:41 27 January 2011

readily attacked by a second hydride. The reaction apparently proceeds by initial attack of hydride at the unsubstituted C-3 or C-5 position and formation of a 3-pyrazoline intermediate (**3**). The second hydride attack at C-5 or C-3 may occur with preliminary Lewis acid initiated isomerization leading to the final pyrazolidine (**2**) (Scheme 1). Although, 3-pyrazolines have been reported to be stable toward CMH,[2] they are readily reduced to pyrazolidines by the combination of $LiAlH_4$ with $AlCl_3$. In some cases the reaction stops at first stage of the proposed pathway giving 3-pyrazolines (**3** and **4**) as the only products.

The reaction of **1b** with lithium tri-*t*-butoxyaluminium hydride (LTBH) also affords a small amount of the 2-pyrazoline (**5b**). The formation of **5b** could be explained according to the general mechanism outlined in Scheme 1. Similar dequaternizations involving Hofmann eliminations or hydrogenolysis of the $\overset{+}{\mathrm{N}}\text{-}C_2H_5$ bond have been previously reported.[3] Physical constants and spectral data for pyrazolidines (**2**), 3-pyrazolines (**3** and **4**) and 2-pyrazolines (**5**) are given in Table 2.

TABLE 2. Pyrazolidines (**2**), 3-Pyrazolines (**3** and **4**) and 2-Pyrazolines (**5**)

Product[a]	mp[b] (°C)	IR(nujol or film) (cm^{-1})	^{1}H NMR	(CDCl$_3$/TMS	δ [ppm][c]	J [Hz]	
			R^2	R^3	3-H	4-H	5-H
2a	Oil[d]	—	1.10 (d, 3H, J = 6.5)	—	2.90 (m, 1H)	1.85 (m, 2H)	2.60 (m, 2H)
2a•BH$_3$	184-185 (ethanol)	2400 (B-H)	1.25 (d, 3H, J = 6.5)	—	2.80 (m, 1H)	1.70 (m, 2H)	3.30 (m, 3H)
2b	oil[d]	—	1.40 (d, 3H, J = 6)	—	3.05 (m, 1H)	2.20 (m, 2H)	3.40 (m, 2H)
2c	oil[d]	—	—	1.40 (d, 3H, J = 6)	2.80 (m, 2H)	2.10 (m, 2H)	3.55 (m, 1H)
2e	oil[d]	—	—	—	2.90 (t, 2H, J = 7)	2.15 (m, 2H)	3.45 (t, 2H, J = 7)
3b	oil[d]	1670 (C=C)	1.70 (s, 3H)	—	—	5.55 (t, 1H, J = 5)	4.00 (d, 2H, J = 5)
4b	oil[d]	1650 (C=C)	1.10 (d, 3H, J = 6)	—	6.65 (m, 1H)	4.20 (m, 1H)	3.50 (m, 1H)
4d	84-85 (ethanol)	1620 (C=C)	—	7.00 (s, 5H)	—	5.70 (t, 1H, J = 2.5)	3.60 (d, 2H, J = 2.5)
5b	75-76[e] (hexane)	1550 (C=N)	2.10 (t, 3H, J = 1.2)	—	—	2.70 (m, 2H)	3.60 (m, 2H)

a) Yields of isolated products are listed in Table 1. b) Uncorrected. c) δ 2.40 (s, 3H, N-CH_3), 2.60-2.90 (q, 2H, J = 7, N-CH_2CH_3), 1.05 (t, 3H, J = 7, N-CH_2CH_3), 6.90-7-10 (m, 5H, N-C_6H_5). d) Unstable oily compound. e) lit.[5] mp. 76-77°(ether or ligroin).

EXPERIMENTAL SECTION

Melting points were determined on a Buchi apparatus and are uncorrected. IR spectra were recorded using a Pye-Unicam SP1100 spectrometer and the ^{1}H NMR spectra were performed on a Varian T-60 instrument; chemical shifts are expressed in ppm relative to TMS as internal standard.

2-Ethyl-1,3-dimethylpyrazolidine (2a). Typical Procedure.- A solution of 2-ethyl-1,3-dimethylpyrazolium tetrafluoroborate[4] (**1a**, 2.1 g, 10 mmol) in ethanol (20 mL) was added to a suspension of sodium borohydride (0.75 g, 20 mmol) in ethanol (20 mL). The mixture was stirred at 25° for 6 hrs., acidified with a saturated NH_4Cl solution (30 mL), and then extracted with ether (2x25 mL). The organic layer was dried over $MgSO_4$ and the solvents removed. The crude product was chromatographed on silica gel using dichloromethane as eluent to give 1.01 g (79%) of **2a** as a colorless oil.

2-Ethyl-3-methyl-1-phenyl-3-pyrazoline (3b) and 1-Ethyl-5-methyl-2-phenyl-3-pyrazoline (4b). Typical Procedure.- A solution of 2-ethyl-3-methyl-1-phenylpyrazolium tetrafluoroborate[4] (**1b**, 2 g, 7.2 mmol) in ether was added to a suspension of lithium aluminium hydride (0.27 g, 7.2 mmol) in ether (20 mL). The mixture was stirred at room temperature for 4 hrs. and hydrolyzed with saturated NH_4Cl (20 mL). The ethereal layer was separated and dried over $MgSO_4$. Evaporation of the solvent left an oil which was chromatographed on silica gel using dichloromethane as eluent. The following compounds were obtained: 2-ethyl-3-methyl-1-phenyl-3-pyrazoline (**3b**) as a colorless oil from the first fraction; yield: 0.67 g (50%). 1-Ethyl-5-methyl-2-phenyl-3-pyrazoline (**4b**) as a colorless oil from the second fraction; yield: 0.40 g (30%).

Downloaded At: 09:41 27 January 2011

TABLE 3. Elemental Analysis Data

Product No.		Elemental Analysis (Found)		
2a	Calcd.	C 65.58 (65.45)	H 12.56 (12.48)	N 21.85 (21.93)
2a.BH$_3$	Calcd.	C 59.19 (59.26)	H 13.47 (13.51)	N 19.72 (19.60)
2b	Calcd.	C 75.75 (75.87)	H 9.52 (9.43)	N 14.72 (14.59)
2c	Calcd.	C 75.75 (75.64)	H 9.52 (9.61)	N 14.72 (14.79)
2e	Calcd.	C 74.96 (74.84)	H 9.14 (9.07)	N 15.89 (15.95)
3b	Calcd.	C 76.56 (76.70)	H 8.55 (8.38)	N 14.87 (14.76)
4b	Calcd.	C 76.56 (76.43)	H 8.55 (8.62)	N 14.87 (14.96)
4d	Calcd.	C 81.56 (81.65)	H 7.24 (7.11)	N 11.19 (11.24)

Acknowledgement.- The authors are indebted to Comisión Asesora de Investigación Cientifica y Técnica for financial Support (Grant PB86-0329).

REFERENCES

1. A. Alberola, L. A. Bañuelos, P. Cuadrado, A. M. González and F. J. Pulido, *Org. Prep. Proced. Int.*, **21**, 237 (1989). This reaction was first reported by J. L. Aubagnac, J. Elguero, R. Jacquier and D. Tizané, *Tetrahedron Lett.*, 3705 (1967).
2. J. L. Aubagnac, J. Elguero and R. Jacquier, *Bull. Soc. Chim. France*, 3306 (1969).
3. M. P. Cooke, Jr. and R. M. Parlman, *J. Org. Chem.*, **40**, 531 (1975).
4. Pyrazolium salts were prepared by standard procedures: R. B. Woodward and R. A. Olofson, *Tetrahedron Suppl.*, **7**, 415 (1966).
5. I. Heilbron, "*Dictionary of Organic Compounds*", Eyre and Spottiswoode, London, 1965.

****

Downloaded At: 09:41 27 January 2011

A CONVENIENT PREPARATION OF 5,5-DIALKYL MELDRUM'S ACIDS

Submitted by
(08/21/91)

Bang-Chi Chen[†] and Ping Lue*[††]

[†] *Department of Chemistry*
Drexel University, Philadelphia, PA 19104

[††] *Occidental Chemical Corporation, Technology Center*
2801 Long Road, Grand Island, NY 14072

Meldrum's acid (**1**, 2,2-dimethyl-1,3-dioxane-4,6-dione, isopropylidene malonate), discovered by Meldrum,[1] is an attractive alternative to acyclic malonate esters in organic synthesis.[2] 5,5-Dialkyl Meldrum's acids are versatile synthetic intermediates and their applications in organic transformations have been amply demonstrated and well documented.[2,3] As a consequence, many efforts have been aimed at developing efficient methods for the preparation of these synthetically useful compounds.[2,4] On the other hand, however, each of the existing methods suffers one or another disadvantages such as low yield, apparently resulting from the hydrolytic ring-opening by the base employed; or tedious, often chromatographic separation of products. We now report a convenient method for preparation of 5,5-dialkyl Meldrum's acids (**2**) based on our recent observation that triethylamine in dimethyl sulfoxide acts as a homogeneous, but strong enough base in the reaction of Meldrum's acid with carbon disulfide.[5]

When treated with triethylamine in dimethyl sulfoxide, Meldrum's acid (**1**) reacts readily with alkyl halides[6] at room temperature to afford 5,5-dialkyl Meldrum's acids (**2**). The reaction is convenient, involving stirring of the reaction mixture at room temperature. Since the reaction gives high yield (>90%) of product, work-up becomes very simple. Addition of water to the reaction