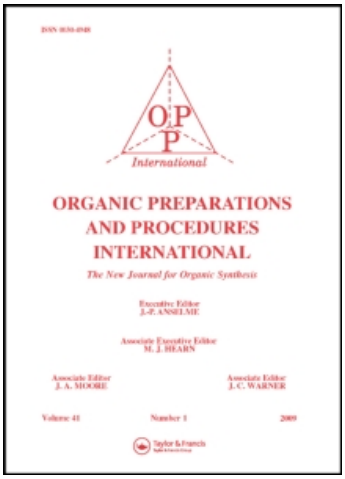

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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Li Xin Wang[a]; Yao Zeng Shi[a]; Ming Hua Xu[a]; Hong Wen Hu[a]
[a] Department of Chemistry, Nanjing University, Nanjing, PR CHINA

To cite this Article Wang, Li Xin , Shi, Yao Zeng , Xu, Ming Hua and Hu, Hong Wen(1996) 'CONDENSATION OF 1,4-DIACETYL-2,5-PIPERAZINEDIONE WITH ALDEHYDES PROMOTED BY ULTRASONICALLY DISPERSED POTASSIUM', Organic Preparations and Procedures International, 28: 2, 226 — 230
To link to this Article: DOI: 10.1080/00304949609356527
URL: http://dx.doi.org/10.1080/00304949609356527

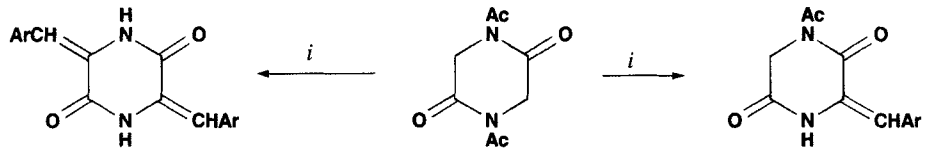
CONDENSATION OF 1,4-DIACETYL- 2,5-PIPERAZINEDIONE WITH ALDEHYDES PROMOTED BY ULTRASONICALLY DISPERSED POTASSIUM†

Submitted by (10/16/95)

Li Xin Wang††, Yao Zeng Shi*, Ming Hua Xu and Hong Wen Hu

Department of Chemistry, Nanjing University
Nanjing 210093, P. R. CHINA

Ultrasound is known to promote a variety of organic reactions, especially those involving metals.[1] Because of the nature of the solvent, these reactions most likely occur on the metal surface; however, this is not always the case with alkali metals especially those of low lattice energy, such as potassium and sodium[2] which, under proper conditions, can be transformed into very fine dispersions. Particles in such a colloidal state may exhibit special effects that occur not only at the interface between metal and solution but also to the slight extension of the metallic phase in the interior of the particles.[3] These considerations suggest that finely dispersed metallic particles in solution may have some useful synthetic properties. Ultrasonically dispersed potassium (UDP, sometimes called colloidal potassium), generated by the sonication of metallic potassium in toluene or xylene,[4,5] has been recognized as a powerful reducing reagent for the cleavage of the C-S bond of cyclic sulfones.[6] It has also been used as an effective reagent for the Dieckmann cyclization of diesters.[4] Recently, we found UDP can be used as both a deprotonating agent and a promoter for the aldol condensation and the Michael reaction for which strong bases(e. g. *t*-BuOK) are required.[7] In view of the many possible modes of reaction and of the "ultrasound" and "dispersion" effects[1b] of UDP, we became interested in exploring its applications and attempted to determine some special characteristics of this "colloidal



5 1 2

a) Ar = Ph b) Ar = 3,4-$(OCH_2O)C_6H_3$
c) Ar = 4-Cl-C_6H_4 d) Ar = 4-F-C_6H_4

i) UDP, ArCHO
ii) UDP, ArCHO, RCHO
iii) MeOH, K_2CO_3

4

a) Ar = Ph, R = Me_2CH
b)*Ar = 4-MeO-C_6H_4, R = Me_2CH
c) Ar = 2-Cl-C_6H_4, R = Me_2CH

3

a) Ar = Ph
b)*Ar = 3,4-$(OCH_2O)C_6H_3$
c)*Ar = 3,4-$(MeO_2)C_6H_3$
d) Ar = 4-$NO_2C_6H_4$
e)*Ar = PhCH=CH (*trans*)

* new compound

reagent".[4] The derivatives of DAPDO (**1**) have great potential in biochemistry[8] and synthesis[9] and may be obtained by the condensation of aldehydes with piperazinedione (PDO)[10] or with DAPDO using strong bases (e. g. *t*-BuOK),[11] by the use of phosphorus ylide,[12] by microwave irradiation[13] or using phase-transfer catalysis[14] in a few hours to a few days in moderate to excellent yields; however, there remains some problems in these syntheses.[1] We now report the applications of UDP on the aldol condensation of 1,4-diacetyl-2,5-piperazinedione (DAPDO) with aldehydes.

Our results show that this finely dispersed potassium behaves as a Lewis base, acting as a deprotonating agent and a promoter of this aldol condensation; the reaction was complete smoothly within 10-150 minutes in 86-100% yields (Table 1) and thus appears to be the most effective method for this type of reaction to date.

As in the reported procedures,[10-14] monoarylidene and symmetric diarylidene products (**2** and **5**) may be obtained by controlling the amounts of potassium and aldehydes used; however, DAPDO reacted violently with *trans*-cinnamaldehyde, and only **2e**[15] was obtained even then excess aldehyde was used. Since **2** might be partially deacylated when the excess of potassium was destroyed with glacial acetic acid, it was treated with methanol and catalytic potassium carbonate[16] to afford pure **3**. *To obtain the asymmetric products **4**, it is important to allow compound **1** to condense first with equimolar amounts of the aromatic aldehyde, followed with an excess of the aliphatic aldehyde.* The reverse procedure was ineffective even though longer sonication was performed and is currently under investigation.

TABLE 1. Yield, Reaction Time, mp and Elemental Analysis

Cmpd	Yield (%)	mp (°C)	lit. mp (°C)	Time (min)	Elemental Analysis (Found) C	H	N
2e	100	303-304	—	< 2	66.65 (66.48)	5.22 (5.15)	10.37 (10.40)
3a	87	270-272	270-271[17]	30	—	—	—
3b	94	257-258	—	25	58.54 (58.58)	4.09 (4.29)	11.37 (11.29)
3c	91	261-262	—	20	59.54 (59.65)	5.38 (5.40)	10.68 (10.67)
3d	100	272-274	275-278[11]	10	—	—	—
4a	87	267-268	264-265[14b]	150	—	—	—
4b	92	263-264	—	150	67.12 (67.47)	6.34 (6.17)	9.78 (9.46)
4c	86	306-307	308-310[14b]	150	—	—	—
5a	92	303-304	301-302[14b]	60	—	—	—
5b	89	317-319	320-322[14b]	50	—	—	—
5c	96	>360	>360[14b]	50	—	—	—
5d	91	342-345	343-351[14b]	45	—	—	—

EXPERIMENTAL SECTION

Toluene was distilled from sodium. Potassium was freshly cut.[4] Liquid aldehydes were commercially available and were freshly distilled. Other reagents (c.p) were used as purchased without further

purification. Melting points were measured with a Micro Melting Point apparatus and are uncorrected. IR spectra were obtained as KBr pellets on a Shimadzu IR-408 spectrometer. ^{1}H NMR spectra were recorded at 90MHz or 500MHz on a Varian FX-90Q or a Bruker 500 spectrometer using TMS as an internal standard. MS were measured by EI using the VG-ZAB-HS instrument. Elemental Analysis were on a Perkin-Elmer 240C instrument and UV/vis were obtained on a UV-240 spectrometer.

TABLE 2. Spectral Data

Cmpd	IR (cm^{-1})			MS (m/z)	^{1}H NMR[a]
	NH	C=O	C=C	M^+ (%)	
2e	3395	1686	1630	270 (48)	10.7 (1H, NH), 7.65-7.57 (q, 1H, =CH, J_1 = 15Hz, J_2= 12 Hz), 7.57-7.26 (m, 5H, ArH), 6.92, 6.89 (d, 1H, =CH, J = 15 Hz), 6.71, 6.69 (d, 1H, CH=, J = 12Hz), 4.25 (s, 2H, $COCH_2N$), 2.43 (s, 3H, $COCH_3$)
3a	3375 3200	1690	1630	—	10.03 (br, 1H, NH), 8.15 (br, 1H, NH), 7.57-7.15 (m, 5H, ArH), 6.78 (s, 1 H, CH=), 4.25 (s, 2H, $COCH_2N$)
3b	3200 3015	1690	1620	246 (100)	9.66 (br, 1H, NH), 8.09 (br, 1H, NH), 7.10-6.78 (m, 3H, ArH), 6.61 (s, 1H, CH=), 6.02 (s, 2H, OCH_2O), 3.95 (s, 2H, $COCH_2N$)
3c	3300 3150	1680	1630	262 (100)	9.64 (br, 1H, NH), 8.08 (1H, NH), 7.03, 7.00 (d, 3H, ArH), 6.65 (s, 1H, CH=), 3.98 (s, 2H, $COCH_2N$), 3.78 (s, 6H, 2 OCH_3)
3d	3395	1680	1630	—	8.50, 8.47 (d, 1H, ArH, J = 2.7Hz), 8.40, 8.37 (d, 1H, ArH, J = 2.7Hz), 7.77-7.62 (q, 2H, ArH), 7.44 (s, 1H, CH=), 4.57 (s, 2H, $COCH_2N$)
4a	3220	1690	1640	—	7.23 (m, 6H, CH=), 6.23, 6.12 (d, 1H, CH=, J = 10Hz), 2.73 (br, 1H, =CH), 1.23 (d, 6H, $CHMe_2$, J = 6Hz)
4b	3130	1670	1630	286 (100)	7.45, 6.83 (d, 4H, ArH, J = 5Hz), 7.18 (s, 1H, ArCH=), 6.16 (d, 1H, =CH, J = 8Hz), 3.87 (s, 3H, OCH_3), 2.80 (m, 1H, $CHMe_2$), 1.1 6 (d, 6H, $CHMe_2$, J = 5Hz)
4c	3150	1670	1640	—	7.25 (m, 6H, ArCH=), 6.27 (d, 1H, =CH, J = 10Hz), 2.67 (m, 1H, CH), 1.20 (d, 6H, $CHMe_2$, J = 6Hz)
5a	3175	1680	1630	—	7.31 (m, 12H, 2xArCH=)
5b	3200	1690	1640	—	7.20 (m, 6H, ArH), 6.95 (s, 2H, 2xArCH=), 6.05 (s, 4H, 2xOCH_2O)
5c	3200	1690	1630	—	7.51-7.34 (m, 10H, 2xArCH=)
5d	3200	1690	1630	—	7.61-7.02 (m, 10H, 2xArCH=)

a) **2e** was recorded at 500MHz using DMSO-d_6 as solvent, other compounds were recorded at 90MHz using CF_3CO_2D as solvent.

Typical Procedure.- To a toluene solution of UDP (5.2 mmol),[4] a solution of ArCHO (5 mmol) and **1** (5 mmol) in 15 mL dry toluene was added dropwise under N_2 atmosphere at 0° (ultrasound bath filled

with soap and ice-water). Sonication (100W. common cup ultrasound generator was used) was continued until the reaction was complete by TLC. After cooling, about 5 mL of glacial acetic acid was carefully added to the residue. The mixture was cooled again to ambient temperature and water was added. A white solid was obtained by filtration. It was recrystallized from aqueous acetic acid. For the synthesis of compound **5**, 2.2 equiv. potassium and 2.2 equiv. of the aldehydes are needed. For compound **4**, 2.2 equiv. potassium, 1 equiv. aromatic aldehyde was sonicated for 30 minutes, then 2 equiv. of the aliphatic aldehyde was added. The spectral data of the products were listed in Table 2. Compound **2e**, in this case, pure **2** obtained within 2 minutes, UV(MeOH): 230, 315nm.

The synthesis of compounds **5** was performed as described above, using 2.2 equiv. aromatic aldehydes.

The synthesis of compound **4** was carried out as described for compound **3**; sonication was continued for another 10 minutes, then 20 mmol of the freshly distilled aliphatic aldehyde in 20 mL of toluene was added dropwise; again sonication was continued to specified time (Table 1). Work-up was as described above.

Acknowledgment.- We thank the National Nature Science Foundation and the National Education Commission Foundation of China for financial support.

REFERENCES

† Part 1 of Applications of Ultrasonically Dispersed Potassium (UDP).

†† Present address: Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu, 610041, P. R. China.

1. a) C. Einhorn, J. Einhorn and J. L. Luche, *Synthesis*, 787 (**1989**); b) S. V. Ley and C. M. R. Low, *Ultrasound in Synthesis*, Springer Verlag, Berlin, **1989**.

2. J. L. Luche, *Ultrasonics*, **25**, 40 (1987).

3. H. W. Kohlschutter, *"New Synthetic Methods"* Vol 3, p. 1, Verlag Chemie, Wienheim, 1975.

4. J. L. Luche, C. Petrier and C. Duppy, *Tetrahedron Lett.*, **25**, 753 (1984).

5. Solvents are quite important in ultrasonication of metallic dispersions. For example, while potassium can be dispersed both in toluene and xylene, sodium can only be dispersed in xylene. However, neither potassium nor sodium can be dispersed in THF. Lithium which is soft can be hardly dispersed in organic solvents. For discussions see ref. 1b, 2, 4.

6. a) T. S. Chou and M. L. You, *Tetrahedron Lett.*, **26**, 4495 (1985); b) T. S. Chou and M. L. You, *J. Org. Chem.*, **52**, 2224 (1987); c) T. S. Chou and M. M. Chen, *Heterocycles*, **26**, 2829 (1987); d) T. S. Chou, S. H. Hung, M. L. Peng and S. J. Lee, *Tetrahedron Lett.*, **32**, 3551 (1991).

7. L. X. Wang and Y. Z. Shi, Unpublished results.

8. C. Shin, Y. Yonezawa, Y. Sato and T. Nakano, *Heterocycles*, 405 (**1983**).

9. a) H. Maag, J. F. Blount, D. L. Coffin, T. V. Steppe and F. Wong, *J. Am. Chem. Soc.*, **100**, 6786 (1978); b) M. Yamaura, T. Suzuki, H. Hashimoto, J. Yoshimura and C. Shin, *Chemistry Lett.*, 1547 (**1984**).

10. a) T. Sasaki, *Ber.*, **54**, 163 (1921); b) C. Shin, Y. Chigera, M. Masaki and M. Ohta, *Bull. Chem. Soc. Jpn*, **42**, 191 (1969).

11. C. Gallina and A. Liberatori, *Tetrahedron*, 667 (**1974**).

12. D. Person and M. Le Corre, *Bull. Soc. Chim. France*, 673 (**1983**).

13. D. Villemin and A. Ben Alloum, *Synth. Commun.*, **20**, 3325 (1990).

14. a) X. M. Zhou, Y. Z. Shi, Z. M. Du and H. W. Hu, *Chem. J. Chin. Univ.*, **12**, 336(1991); *Chem. Abstr.*, **115**:279956c (1991); b) Z. M. Du, X. M. Zhou, Y. Z. Shi and H. W. Hu, *Chin. J. Chem.*, **10**, 82 (1992), *Chem. Abstr.*, **117**:90238v (1992).

15. Full characterization of this compound: L. X. Wang, Y. Z. Shi and H. W. Hu, *Chin. J. Magn. Reson.*, **12**, 63 (1995).

16. L.X. Wang, Y. Z. Shi and H. W. Hu, *Chin. Chem. Lett.*, **4**, 687 (1993); *Chem. Abstr.*, **121**,9329p (1994).

17. C. Shin, M. Hayakawa, T. Suzuki, A. Ohtsuka and J. Yoshimura, *Bull. Chem. Soc. Jpn*, **51**, 550 (1978).

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SYNTHESIS OF 1,3,6,8-TETRAMETHOXY-*cis*-4b,5,9b,10-TETRAHYDROINDENO[2,1-a]INDENE-5,10-DIONE

Submitted by (08/25/95) D. E. Bianchi, E. N. Alesso and G. Y. Moltrasio Iglesias*

Departamento de Quimica Organica
Facultad de Farmacia y Bioquimica
Universidad de Buenos Aires Junin 956 (1113)
Buenos Aires, ARGENTINA

For use in an investigation of the synthesis of pallidol **8**,[1] an unambiguous synthesis of **7a** was required, and we now describe a synthetic sequence for its preparation.