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Solid State Cleavage of Semicarbazones and Phenylhydrazones with Ammonium Persulfate–Clay using Microwave or Ultrasonic Irradiation

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Abstract: Adsorbed on clay, semicarbazone and phenylhydrazone derivatives are oxidatively cleaved in solid state to generate the corresponding ketones by ammonium persulfate using microwave or ultrasonic irradiation.

Semicarbazones and hydrazones are important intermediates in organic synthesis because of their use in the protection[1-3] and purification[2] of the carbonyl compounds. Extensive studies on the deprotection of these derivatives have been carried out using various catalysts such as copper(II) chloride,[3a] cation exchange resin Dowex-50,[3b] clayfen,[3c] potassium bromate,[3d] and zirconium sulfophenyl phosphonate.[3e] These methods invariably require higher temperatures,[3a,b] longer reaction times and involve toxic metal ions[3e-g] as catalysts which are detrimental to the environment. Consequently, there is a need for the development of protocols using readily available and safer reagents.

In recent years, the organic reactions on solid supports[4] and those that are assisted by microwaves,[5-7] especially under solventless conditions,[6f-j,7] have attracted attention because of their enhanced selectivity, milder reaction conditions and associated ease of manipulation. In continuation of our ongoing efforts in this area,[7] we wish to report a simple oxidative cleavage of semicarbazones and phenylhydrazones with ammonium persulfate and montmorillonite K 10 clay that is accelerated by microwave or ultrasonic irradiation.

Ammonium persulfate is an inexpensive and readily accessible oxidizing agent. It is commonly used in industry for bleaching[8] and for waste water treatment.[9] However, only scanty literature is available that describes its applications in organic synthesis e.g. the oxidation of alkenes[10] and substituted aromatics,[11] cyclization,[12] and deoximation under strenuous conditions using sulfuric acid.[13] Consequently, we decided to explore the oxidative cleavage of the imine-type moieties using ammonium persulfate. In the absence of the mineral supports, the attempted cleavage of semicarbazones failed with ammonium persulfate under both, microwave as well as ultrasonic irradiation conditions even after prolonged reaction periods. In view of the established beneficial effects

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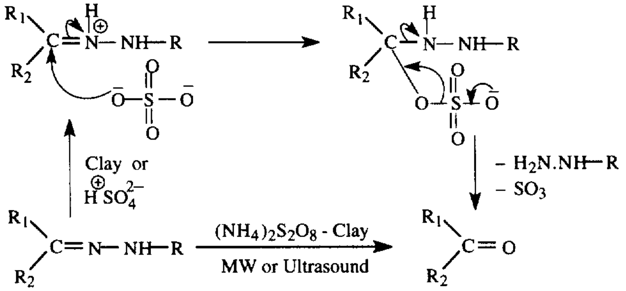
Dedicated to Dr. Paul Anastas for his ceaseless efforts and support of the Green Chemistry initiatives of the reagents on solid supports,[4] we examined a variety of mineral supports such as alumina, clay and silica with ammonium persulfate and soon discovered that montmorillonite K10 clay provides the clean regeneration of the corresponding ketones. The chemoselectivity of the reaction is apparent as the semicarbazone and phenylhydrazone derivatives of aldehydes failed to undergo reaction under the same conditions. When the semicarbazone (entry 1, table), adsorbed on clay is mixed with ammonium persulfate, the reaction is completed in 0.6 min under the influence of microwaves and in 45 minutes under ultrasonic agitation at room temperature. In a separate experiment, the reaction becomes sluggish when all the reactants are mixed together simultaneously.

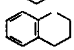
The mechanism of the above transformation probably involves the decomposition of ammonium persulfate on clay (which is acidic and contains water) under the influence of microwaves thus generating O_2 and NH_4HSO_4 (**Eqn.**). The imino nitrogen of the semicarbazone or phenylhydrazone is protonated followed by the second step involving the nucleophilic attack of sulfate ion on the imino carbon. The elimination of semicarbazide and sulfur trioxide liberates the carbonyl compound (**Scheme**).

$$2(NH_4)_2S_2O_8 + 2H_2O \xrightarrow{\Delta} 4NH_4HSO_4 + O_2 \qquad \textbf{(Eqn.)}$$



(Scheme)

Table: Cleavage of semicarbazones and phenylhydrazones with ammonium persulfate and clay using microwave or ultrasonic irradiation.[a]

Entry	R_1	R_2	R	Microwave Time (min)	Microwave Yield[b,c] (%)	Ultrasound Time (h)	Ultrasound Yield[b,c] (%)
1	C_6H_5	CH_3	$CONH_2$	0.6	72	0.75	77
2	*p*-Cl-C_6H_4	CH_3	$CONH_2$	1.8	82	3.00	90
3	*p*-OH-C_6H_4	CH_3	$CONH_2$	1.0	85	1.00	94
4	*p*-Me-C_6H_4	CH_3	$CONH_2$	2.0	69	3.00	68
5	*p*-OMe-C_6H_4	CH_3	$CONH_2$	0.9	78	3.00	88
6	*p*-NH_2-C_6H_4	CH_3	$CONH_2$	1.0	65	1.50	62
7	*p*-OMe-$C_6H_4CH_2CH_2$	CH_3	$CONH_2$	1.6	75	3.00	71
8	$CH_3CH_2CH_2CH_2$	CH_2CH_3	$CONH_2$	1.3	70	2.50	79
9	C_6H_5	CH_3	C_6H_5	0.5	71	1.50	82
10	$CH_3CH_2CH_2CH_2$	CH_2CH_3	C_6H_5	1.3	65	1.00	71
11			$CONH_2$	0.7	68	1.50	69
12			$CONH_2$	1.0	69	2.00	58

[a] Ratio of semicarbazones/phenylhydrazones to ammonium persulfate on clay is 1:8 (molar). [b] Yields refer to pure isolated products. [c] All products are characterized by comparison of their m.p., IR, and NMR spectra with those of the authentic samples.

The deprotection of acetophenone semicarbazone is representative of the general procedure employed. Montmorillonite K10 clay (1.7 g) is added to acetophenone semicarbazone (0.177 g, 1 mmol) that is dissolved in a minimum amount of dichloromethane-methanol. After evaporation of the solvent, the dry powder is mixed with ammonium persulfate (1.82 g, 8 mmol) and the reaction mixture is subjected to microwave irradiation for 0.6 min (as monitored by thin layer chromatography, TLC). The product is extracted into dichloromethane (3x30 mL) and the clay is removed *via* filtration through a sintered glass funnel. The solvent from the combined extracts is removed under reduced pressure and the crude product is passed through a bed of neutral alumina (1 cm) using dichloromethane as an eluent. In case of phenylhydrazones, the residue is chromatographed on a silica gel column using hexane and hexane-dichloromethane (4:1) as the eluents.

Alternatively, the mixture of semicarbazone, clay and ammonium persulfate is transferred into a test tube and subjected to ultrasonic irradiation in a cleaning bath.[14] After completion of the reaction (followed on TLC), the product is purified as described above. Our results for the cleavage of semicarbazone and phenylhydrazone derivatives are compared with those obtained using microwaves and are summarized in the Table.

CAUTION: In view of the hazards associated with an oxidant and evolution of gases during the reaction due caution is recommended for its use at elevated temperatures. We suggest that the microwave oven be operated carefully and for a shorter duration of time because of the possible higher localized temperatures attained.

That the effect may not be purely *thermal* [15] in these reactions is supported by the fact that using an alternate conventional heating mode (oil bath) at the same temperature of 67 °C, the reaction (acetophenone semicarbazone, entry 1) could be completed in 28 h. For comparison, the same reaction under ultrasonic agitation requires 0.6 h to complete. At room temperature and without any exposure to irradiation the reaction gets completed in 72 h using the same amount of oxidant.

In conclusion, we have developed a facile solid state method for the cleavage of semicarbazone and phenylhydrazone derivatives that rapidly regenerates the corresponding ketones using inexpensive ammonium persulfate and clay coupled with irradiation from a microwave or ultrasonic source.

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REFERENCES AND NOTES

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1. a) Loewenthal, H.J.E. in *Protective Groups in Organic Chemistry*; McOmie, J.F.W., Ed; Plenum Press; New York, **1973**, pp 340; b) Kirk, D.N.; Slade, C.J. *Tetrahedron Lett.* **1980**, *21*, 651; c) McGuckin, W.F.; Kendall, E.C. *J. Am. Chem. Soc.* **1952**, *74*, 5811.
2. a) Gillam, A.E.; West, T.F. *J. Chem. Soc.* **1945**, 95; b) Hershberg, E.B. *J. Org. Chem.* **1948**, *13*, 542; Eisenbraun, E.J.; Wesley, R.P.; Budhram, R.S.; Dewprasad, B. *Chem. Ind. (London)* **1989**, 549.
3. a) Ram, R.N.; Varsha, K. *Tetrahedron Lett.* **1991**, *32*, 5829; b) Ranu, B.C.; Sarkar, D.C. *J. Org. Chem.* **1988**, *53*, 878 and references cited therein; c) Laszlo, P.; Polla, E. *Synthesis* **1985**, 439; d) Narayanan,

S.; Srinivasan, V.S. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1557; e) Curini, M.; Rosati, O.; Pisani, E.; Costantino, U. *Synlett* **1996**, 333; f) Butler, R.N.; Morris, G.J.; O'Donohue, A.M. *J. Chem. Res. (S)* **1981**, 61; g) Salmon, M.; Miranda, R.; Angeles, E. *Synth. Commun.* **1986**, *16*, 1827.

4. a) Clark, J.H. *Catalysis of Organic Reactions by Supported Inorganic Reagents*, VCH publisher, Inc., NY **1994**; b) Balogh, M.; Laszlo, P. *Organic Chemistry Using Clays*, Springer-Verlag, Berlin **1993**; c) Smith, K. *Solid Supports and Catalyst in Organic Synthesis*, Ellis Horwood, Chichester, **1992**; d) Laszlo, P. *Preparative Chemistry Using Supported Reagents*, Academic Press, Inc. San Diego, **1987**; e) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909; f) McKillop, A.; Young, D.W. *Synthesis* **1979**, 401; 481; g) Posner, G.H. *Angew. Chem.* **1978**, *90*, 527; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 487; h) Clark, J.H.; Ross, J.C.; Macquarrie, D.J.; Barlow, S.J.; Bastock, T.W. *Chem. Commun.* **1997**, 1203.
5. For recent reviews on microwave-assisted chemical reactions, see a) Abramovich, R.A. *Org. Prep. Proced. Int.* **1991**, *23*, 683; b) Whittaker, A.G.; Mingos, D.M.P. *J. Microwave Power Electromagn. Energy* **1994**, *29*, 195; c) Majetich, G.; Hicks, R. *J. Microwave Power Electromagn. Energy* **1995**, *30*, 27; d) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; e) Strauss, C.R.; Trainor, R.W. *Aust. J. Chem.* **1995**, *48*, 1665; f) Varma, R.S. *"Microwave-Assisted Reactions under Solvent-Free 'Dry' Conditions"* in *Microwaves: Theory and Application in Material Processing IV,* Clark, D.E.; Sutton, W.H.; Lewis, D.A. Eds., American Ceramic Society, Ceramic Transactions **1997**, *80*, pp 375-365; g) For commentary on the First World Congress on Microwave Processing, see Dagani, D. *Chem. Eng. News* February 10, **1997**, p. 26.
6. a) Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986**, *27*, 279; b) Giguere, R.J.; Bray, T.L.; Duncan, S.M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945; c) Bose, A.K.; Manhas, M.S.; Ghosh, M.; Raju, V.S.; Tabei, K. *Heterocycles* **1990**, *30*, 741; d) Bose, A.K.; Manhas, M.S.; Ghosh, M.; Shah, M.; Raju, V.S.; Bari, S.S.; Newaz, S.N.; Banik, B.K.; Chaudhary, A.G.; Barakat, K.J. *J. Org. Chem.* **1991**, *56*, 6968; e) Bose, A.K.; Jayaraman, M.; Okawa, A.; Bari, S.S.; Robb, E.W.; Manhas, M.S. *Tetrahedron Lett.* **1996**, *37*, 6989; f) Bosch, A.I.; Cruz, P.; Diez-Barra, E.; Loupy, A.; Langa, F. *Synlett* **1995**, 1259; g) Oussaid, A.; Thach, L. N.; Loupy, A. *Tetrahedron Lett.* **1997**, *38*, 2451; h) Benalloum, A.; Labiad, B.; Villemin, D. *J. Chem. Soc., Chem. Commun.* **1989**, 386; i) Villemin, D.; Labiad, B. *Synth. Commun.* **1990**, *20*, 3325; 3333; j) Villemin, D.; Benalloum, A. *Synth. Commun.* **1991**, *21*, 1; 63.
7. a) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3207; b) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 4603; c) Varma, R.S.; Varma, M.; Chatterjee, A.K. *J. Chem. Soc., Perkin. Trans. 1* **1993**, 999; d) Varma, R.S.; Lamture, J.B.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3029; e) Varma, R.S.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997**, *38*, 2039; f) Varma, R.S.; Dahiya, R. *Tetrahedron Lett.* **1997**, *38*, 2043; g) Varma, R.S.; Saini, R.K. *Tetrahedron Lett.* **1997**, *38*, 2623; h) Varma, R.S.; Saini, R.K. *Tetrahedron Lett.* **1997**, *38*, 4337; i) Varma, R.S.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997**, *38*, 5131; j) Varma, R.S.; Saini, R.K.; Meshram, H.M. *Tetrahedron Lett.* **1997**, *38*, in press; k) Varma, R.S.; Meshram, H.M. *Tetrahedron Lett.* **1997**, *38*, 5427; l) Varma, R.S.; Saini, R.K. *Synlett.* **1997**, 857.
8. Kazunobu, N.; Kanetsugu, T. *Japan patent Appl.* 71 96,636; *Chem. Abstr.* **1974**, *80*, 16373m.
9. Zumbrunn, J.P. *Trib. CEBEDEAU* **1973**, *26*, 332; *Chem. Abstr.* **1974**, *80*, 19176k.
10. Fristad, W.E.; Peterson, J.R. *Tetrahedron Lett.* **1983**, *24*, 4547.
11. Clerici, A.; Porta, O. *Can.J. Chem.* **1980**, *58*, 2117.
12. Tryupina, V.M.; Almaev, R.Kh.; Bikkulov, A.Z.; Kalinina, V.M.; Baiguzina, G.A. *USSR SU* 1,198,073; *Chem. Abstr.* **1986**, *105*, 152926f.
13. Brooks, S.G.; Evans, R.M.; Green, G.F.H.; Hunt, J.S.; Long, A.G.; Mooney, B.; Wyman, L.J. *J. Chem. Soc.* **1958**, 4614.
14. Ultrasonic cleaning bath (Bransonic, model 3210) was used at room temperature.
15. For a critical evaluation of activation process by microwaves see: Raner, K.D.; Strauss, C.R.; Vyskoc, F.; Mokbel, L. *J. Org. Chem.* **1993**, *58*, 950. The temperature of the reaction mixture inside the alumina bath (heat sink) in a Sears Kenmore microwave oven (2450 MHz) at its full power level (800 Watts) reached ~67 °C after 0.6 min of irradiation.

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