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Communications

Facile Synthesis of Multiple Ketones from α-Oximinoketones Using Dinitrogen Tetroxide

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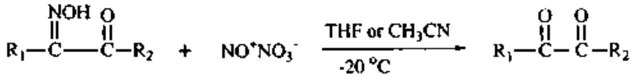
After the first discovery of diphenyl triketone by de Neufville and von Pechmann in 1890,[1] the question that how many carbonyl groups may be juxtaposed and what will be the properties of the resulting vicinal poly ketones is raised and has continued through the years. No polyketone containing more than four vicinal carbonyl group as free form has been reported, although such compound could certainly be capable of existence.[2] 1,2-Dicarbonyl and tricarbonyl compounds are usually obtained by the oxidation of ketones and aldehydes containing active α-methyl or methylene groups[3] or hydrolysis of α,α-dihalides which are formed by the halogenation of active methylene groups.[3,4] Typical agents for the oxidation of active methylene groups are molecular oxygen (autoxidation),[3] potassium superoxide,[5] potassium permanganate.[3] It was also reported that nitrosating agents such as nitrous acid, alkyl nitrite, and organic nitroso compound can be used to convert α-methyl or α-methylenic carbonyl compounds into 1,2-dicarbonyl derivatives through α-oximino ketone intermediate with some degree of sucess.[3,6] However, 1,3-dicarbonyl compounds react with nitrous acid to form trinitroso compounds, but the isolation of tricarbonyl compounds from such systems has not been reported. Since oximes and hydrazones such as N,N-dimethyl-, phenyl-, 2,4-dinitrophenyl hydrazones can be employed as ketone or aldehyde functional group equivalents in organic synthesis,[7] a number of methods have been developed to bring about such conversion reaction.[8] Most require strongly oxidizing or reducing conditions, basic or acidic media. Olah *et al.* have reported the oxidative clevage of oximes in CH_2Cl_2 with aqueous bromine buffered with sodium hydrogen carbonate at room temperature.[9] Laszlo *et al.* reported the carbonyl regeneration from hydrazones by using Clay-supported iron (III) nitrate which was a source of nitrosonium ion(NO^+).[10] Previously, we have also reported the conversion of oximes and hydrazones into their corresponding carbonyl compounds by reacting with dinitrogen tetroxide in aprotic solvent such as THF or CH_3CN under mild conditions.[11]



$$R_1-\overset{NOH}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-R_2 + NO^+NO_3^- \xrightarrow[-20\,^\circ C]{\text{THF or } CH_3CN} R_1-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-R_2$$

Scheme 1.

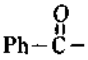
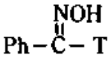
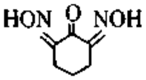
We have now found that α-oximino carbonyl compounds reacted with dinitrogen tetroxide under mild conditions to give 1,2-diketones and 1,2,3-triketones. α-Oximino carbonyl compounds can be easily prepared from ketones containing active α-methylene groups with alkyl nitrite[12] or t-butyl thionitrate.[13]

In a typical procedure,[14] dinitrogen tetroxide solution (2.5 mmol, CCl_4: 300 μl) was slowly added to the α-oximino-3-phenyl-3-propanone (163 mg, 1 mmol) in anhydrous tetrahydrofuran (5 ml) at −20℃ with good stirring. The reaction was monitored by t.l.c. (Kiesegel $60F_{254}$, ether : *n*-hexane = 1 : 1). After stirring for 40 min., 25 ml of ether was added to the reaction mixutre and the ether layer was twice washed with 10 ml of saturated sodium bicarbonate solution to remove the resulting acid and then, dried over anhydrous magnesium sulfate. After evaporation of the solvent, the reaction mixture was separated by column chromatography (Silicagel, Wako gel 300, ether : *n*-hexane = 1 : 2) to give the pure 1-phenyl-1,2-propanedione (115 mg, 78%). All the products thus obtained were identified by comparing their IR, ^1H NMR spectra and physical datas with those from the authentic samples. The results obtained are summarized in Table 1.

N_2O_4 is known to be in equilibrium with NO^+ and NO_3^- in solution by its self ionization, and degree of ionization increases with the dielectric constant of the solvent.[20] The probable reaction mechanism is as follows.

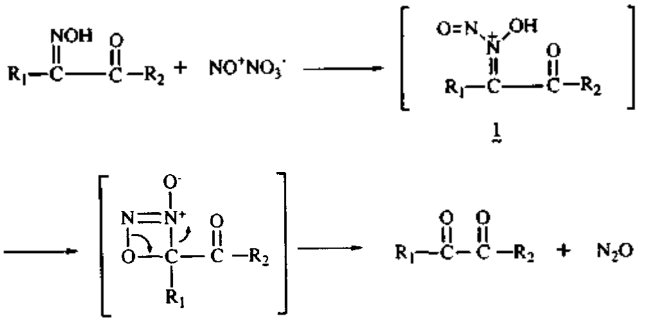
The reaction appears to be initiated by nitrosation on nitrogen atom as shown in Scheme 2. The *N*-nitroso interme-

Table 1. Reaction of α-Oximinoketones with N_2O_4

R_1	R_2	Solvent	N_2O_4 eq.	Reaction Time(min.)	Yield(%)[a]	Ref. No.[b]
Ph	CH_3	THF	2.5	40	72	15
Ph	CH_3	CH_3CN	3	40	64	
CH_3	Ph	THF	2.5	40	78	15
CH_3	Ph	CH_3CN	3	60	63	
$PhCH_2$	Ph	CH_3CN	3	60	73	16
Ph	Ph	THF	3	60	77	17
Ph	Ph	CH_3CN	3	60	75	
 $Ph-\overset{O}{\overset{\|}{C}}-$	Ph	THF	2.5	60	71	18
Ph	 $Ph-\overset{NOH}{\overset{\|}{C}}-$	THF	5	60	62	18
		THF	5	40	76	19
		CH_3CN	6	40	73	

[a] Isolated and purified yield.

[b] References for the known products of ketones are cited in the reference section.



2

Scheme 2.

diate (1) seems rapidly to be converted to the product *via* intermediate (2).[21] The yields of 1,2-diketones and 1,2,3-triketones are comparatively high when the reaction temperatures are controlled at low temperature (below 0℃).

This method can be carried out in the wide range of the low reaction temperature (0℃ ~ −40℃) for short reaction time (30 min.~1 h.) and is simple for work-up after completion of the reaction. Thus, this method can be widely applicable to the synthesis of the various multiple ketones.

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References

1. R. de Neufvile and H. von Pechmann., *Ber.*, **23**, 3375 (1890).
2. M. B. Rubin, *Chem. Rev.*, **75**(2), 177 (1975).
3. C. F. Cullis and A. Fish, "The Chemistry of The Carbonyl Groups", S. Patai ed., Interscience-Wiley, London, Chap. 2, pp. 79-176 (1966).
4. P. Salomaa, "The Chemistry of The Carbonyl Groups", S. Patai ed., Interscience-Wiley, London, Chap. 3, pp. 177-210 (1966).
5. M. Hocquaux and B. Jcquet, *Tetrahedron Lett.*, **25**, 533 (1984).
6. D. T. Manning and H. A. Stansbury, Jr., *J. Am. Chem. Soc.*, **81**, 4885 (1959).
7. (a) A. Mckillop, J. D. Hunt, R. D. Naylor, and E. C. Taylor, *J. Am. Chem. Soc.*, **93**, 4918 (1971); (b) G. Rosini, *J. Org. Chem.*, **39**, 3504 (1974); (c) G. Rosini, R. Ballini, and V. Zanotti, *Synthesis*, 137 (1983); (d) J. K. Whitesell and M. A. Whitesell, *Synthesis*, 517 (1983).
8. (a) E. J. Corey and J. E. Richman, *J. Am. Chem. Soc.*, **92**, 5276 (1970); (b) T. L. Ho and G. A. Olah, *Synthesis*, 611 (1976); (c) D. H. R. Barton, D. J. Lester, and S. V. Ley, *J. Chem. Soc. Chem., Comm.*, 445 (1977); (d) J. R. Maloney, R. E. Lyle, J. E. Saavedra, and G. G. Lyle, *Synthesis*, 212 (1978).
9. G. A. Olah, Y. D. Vankar, and G. K. Surya Prakash, *Synthesis*, 113 (1979).
10. P. Laszlo and E. Polla, *Tetrahedron Lett.*, **25**, 3309 (1984).
11. S. B. Shim, K. Kim, and Y. H. Kim, *Tetrahedron Lett.*, **28**(6), 645 (1987).
12. (a) W. H. Hartung and F. Crossley, *Org. Syn. Coll. Vol*, **II**, 363 (1943); (b) A. F. Ferris, *J. Org. Chem.*, **24**, 1726 (1959); (c) A. F. Ferris, *J. Org. Chem.*, **25**, 12 (1960); (d) A. F. Ferris, G. S. Johnson, and F. E. Gould, *J. Org. Chem.*, **25**, 496 (1960).
13. Y. H. Kim, Y. J. Park, and K. Kim, *Tetrahedron Lett.*, **30**, 2833 (1989).
14. In the case of diphenyl triketone, the reaction mixture was directly condensed to remove solvent and excess N_2O_4, and serarated to give triketone by prep. T.L.C. (Merck, Kieselgel $60F_{254}$, dried ether : *n*-hexane = 1 : 1) under N_2 atmosphere.
15. W. D. Emmons and J. P. Freeman, *J. Am. Chem.*, **77**, 4415 (1955).
16. B. A. Belinka, Jr., and A. Hassner, *J. Org. Chem.*, **44**(25), 4712 (1979).
17. H. T. Clarke and E. E. Dreger, *Org. Syn., Coll. Vol.* **I**, 87 (1941).
18. L. A. Bigelow and R. S. Hanslick, *Org. Syn., Coll. Vol.* **II**, 244 (1943).
19. 1,2,3-Cyclohexanetrione was obtained as dihydrate; B. Pecherer, L. M. Jampolsky, and H. M. Wuest, *J. Am. Chem. Soc.*, **70**, 2587 (1948).
20. W. R. Angus, R. W. Jones, and G. O. Phillips, *Nature*, **164**, 433 (1949).
21. A similar cleavage of C=S bond of thioamides to C=O bond of amides has been reported; see H. J. Kim and Y. H. Kim, *Synthesis*, 970 (1986).