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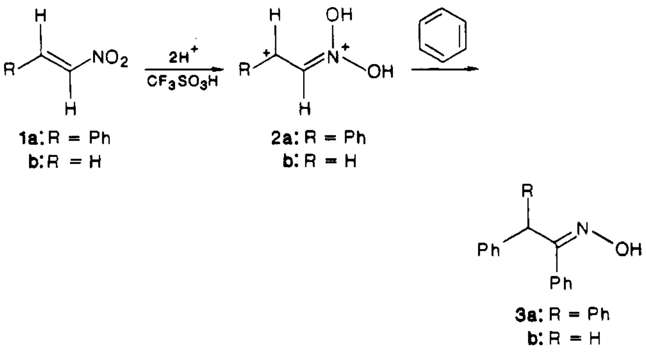
Communications

Novel Electrophilic Species Equivalent to α-Keto Cations. Reactions of O,O-Diprotonated Nitro Olefins with Benzenes Yield Arylmethyl Ketones[1]

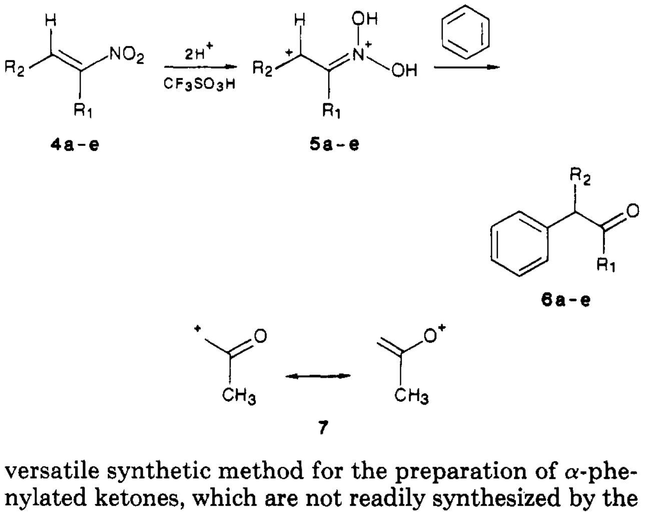
Summary: The *N,N*-dihydroxyiminium carbenium ions formed by O,O-diprotonation of nitro olefins in a strong acid, trifluoromethanesulfonic acid (TFSA), are discrete and novel dipositively charged species. The dications formed from α-substituted nitroethylenes are reactive electrophiles to give α-arylated ketones in high yields. This constitutes a versatile synthetic method for the preparation of α-arylated ketones, which are difficult to synthesize by the conventional Friedel–Crafts reactions.

Sir: Diprotonation of nitro groups in a strong acid, trifluoromethanesulfonic acid (TFSA), is a novel phenomenon, which was discovered for the first time in nitrophthalenes.[2] Recently we have investigated the protonation of nitro groups of nitrostyrenes (**1a**). Based on the value of the cryoscopic constant of TFSA, it was concluded that O,O-diprotonated β-nitrostyrenes (e.g. *N,N*-dihydroxyiminium benzyl dication **2a**) are formed in TSFA (Scheme I).[3] A further study described the reaction of the novel reactive electrophiles.[4] Some dications **2** are stable for hours under suitable conditions, even at 0 °C. We have also presented the surprising result that even a simple nitro olefin (nitroethylene **1b** for example) is also diprotonated in TFSA to form the *N,N*-dihydroxyiminium carbenium dication **2b**.[5] This suggests the intrinsic stabilization of the dications. In the reaction with benzene, the dication **2a** gave diphenylacetophenone oxime (**3a**) in a quantitative yield. The reaction of the dications formed from nitroethylene **1b** with benzene also gave the corresponding diphenylated oxime **3b**.[5] Now, we report a novel reaction, which leads to 3-phenylpropan-2-one (**6a**) from the O,O-diprotonated dication **5a** formed from 2-nitropropene **4a** (Scheme II and Table I). This constitutes a versatile synthetic method for the preparation of α-phenylated ketones, which are not readily synthesized by the conventional Friedel–Crafts reactions.[6,7]

Scheme I



Scheme II



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[1] Portions of this work were presented at the 3rd Chemical Congress of North America, Toronto, Canada, June 1988 (abstract ORGN 344).

[2] Ohta, T.; Shudo, K.; Okamoto, T. *Tetrahedron Lett.* **1984**, *25*, 325.

[3] Ohwada, T.; Ohta, T.; Shudo, K. *J. Am. Chem. Soc.* **1986**, *108*, 3029.

[4] Ohwada, T.; Ohta, T.; Shudo, K. *Tetrahedron* **1987**, *43*, 297.

[5] Ohwada, T.; Itai, A.; Ohta, T.; Shudo, K. *J. Am. Chem. Soc.* **1987**, *109*, 7036.

[6] Unsuccessful Friedel–Crafts reactions were described in (a) Ruggli, P.; Dahn, H.; Wegmann, J. *Helv. Chim. Acta* **1946**, *29*, 113. (b) Richard, G. *C. R. Acad. Sci.* **1935**, *200*, 753. Richard, G. *Bull. Soc. Chim. Fr.* **1938**, 286. A previous investigation of the Friedel–Crafts reaction of nitro olefins were described in Lambert, A.; Rose, J. D.; Weedon, B. C. L. *J. Chem. Soc.* **1949**, 42.

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Table I. Synthesis of α-Phenylmethyl Ketones from Nitro Olefins

nitro olefin	R_1	R_2	temp, °C	time	α-phenylmethyl ketone	yield, %
4a	CH_3	H	−40	1 min	**6a**	85
4b	C_2H_5	H	−40	1 min	**6b**	87
4c	$(CH_2)_4$		−40	2 h	**6c**	72
4d	CH_3	Ph	−40	5 min	**6d**	65
4e	Ph	H	−50	30 min	**6e**	37[a]

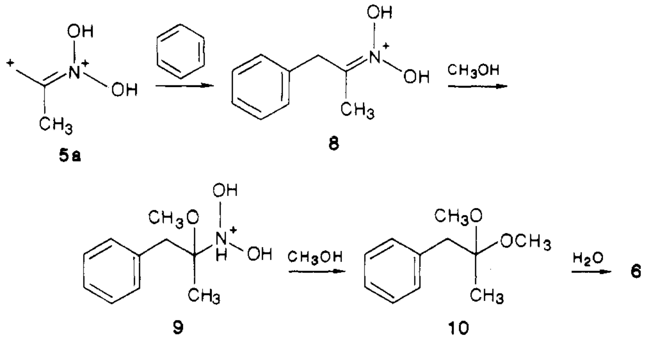
[a] Deoxybenzoin oxime was also obtained in 29% yield.

Table II. Synthesis of α-Arylmethyl Ketones fro 2-Nitropropene (4a)

nitro olefin	ArH	temp, °C	time, min	α-arylmethyl ketone	yield, %
4a	anisol	−40	1	**11a**	93 (o/p = 1/0.42)[a]
4a	toluene	−40	1	**11b**	92 (o/p = 1/1.35)[a]
4a	chlorobenzene	−40	30	**11c**	92 (o/p = 1/2.5)[a]
4a	DMEB[b]	−40	10	**11d**	75
4a	*p*-xylene	−40	10	**11e**	85
4a	naphthalene	−40	10	**11f**	86 (1-naphthyl)

[a] The ortho/para ratios of the products were determined from ^1H NMR spectra. [b] DMEB = 1,4-dimethoxybenzene.

Scheme III



In a typical procedure, a solution of 2-nitropropene (**4a**) (300 mg) in benzene (total amount of benzene used was 30 equiv) was added to a well-stirred solution of TFSA (10 equiv with respect to **4a**) and benzene with co-solvent of methylene chloride cooled to −40 °C in a dry ice–acetone bath. The reaction mixture was immediately (after 1 min) poured into large excess dry methanol (100 mL) cooled to −78 °C with vigorous stirring.[8] After being warmed to the abmient temperature (10–15 min), the yellow solution was diluted with water (150 mL), neutralized with powdered $NaHCO_3$, and saturated with NaCl. The solution was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated, and the residue was flash chromatographed (SiO_2) to give pure 3-phenylpropan-2-one (**6a**) (85% yield).[9] The general applicability of the reaction for the preparation of α-phenylmethyl ketones (**6**) from nitro olefins (**4**) is demonstrated in Table I.

Cryoscopic and NMR spectroscopic studies demonstrate that nitro olefins are diprotonated on their nitro groups in TFSA to give *N*,*N*-dihydroxyiminium carbenium dications as discrete species.[3,5] In the reaction illustrated by Scheme II, the dication can be regarded as an α-keto cation equivalent **7**: the dication **5a** reacted with benzene to give α-phenylated protonated *aci*-nitro compound **8**. While the iminium intermediate formed from nitro olefin, which bears a hydrogen atom at the C_1 carbon atom (in the case of 1-nitroethylene), reacts with another benzene to give a diphenylated oxime,[5] the intermediate whose iminium center was stabilized by an electron-donating group (CH_3) **8** was stable at low temperature. The treatment of the intermediate solution with methanol, followed by the aqueous workup, quantitatively converted the protonated *aci*-nitro compound **8** to the corresponding carbonyl compound by a similar reaction mechanism to the Nef reaction[10] (**8** → **9** → **10**) through a ketal intermediate **10**, which could be isolated by careful workup (Scheme III). These novel electrophilic reagents are reasonably utilized in the synthesis of arylmethyl ketones (**11**) by reaction with substituted aromatic compounds. The yields are high, even in the case of chlorobenzene, for the reaction of 2-nitropropene **4a**, as shown in Table II.

In summary, we have established a versatile synthetic reaction for arylmethyl ketones utilizing novel electrophilic reagents, *N*,*N*-dihydroxyiminium carbenium ions, which are synthetically equivalent to α-keto cations **7**.

Registry No. **4a**, 4749-28-4; **4b**, 2783-12-2; **4c**, 2562-37-0; **4d**, 705-60-2; **4e**, 5468-44-0; **6a**, 103-79-7; **6b**, 1007-32-5; **6c**, 1444-65-1; **6d**, 781-35-1; **6e**, 451-40-1; *o*-**11a**, 5211-62-1; *p*-**11a**, 122-84-9; *o*-**11b**, 51052-00-7; *p*-**11b**, 2096-86-8; *o*-**11c**, 6305-95-9; *p*-**11c**, 5586-88-9; **11d**, 831-29-8; **11e**, 53291-89-7; **11f**, 33744-50-2; benzene, 71-43-2; anisol, 100-66-3; toluene, 108-88-3; chlorobenzene, 108-90-7; *p*-xylene, 106-42-3; naphthalene, 91-20-3; deoxybenzoin oxime, 952-06-7; 2,4-dimethoxybenzene, 151-10-0.

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