Tetrahedron Vol. 43, No 1, pp. 275 to 279, 1987
Printed in Great Britain

0040-4020/87 \$5.00+.00

STUDIES ON THE REDUCTION OF CYCLIC 1,3-DIKETONES VIA THEIR TRIFLATES

A. García Martínez*[a], R. Martínez Alvarez[a], M. Madueño Casado[a],
L. R. Subramanian[b] and M. Hanack*[b]
[a]Departamento de Química Orgánica, Facultad de Ciencias Químicas,
Universidad Complutense, E-28040 Madrid, Spain
[b]Institüt für Organische Chemie, Lehrstuhl für Organische Chemie II
der Universität Tübingen, Auf der Morgenstelle 18, D-7600 Tübingen 1,
West Germany

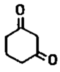
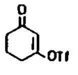
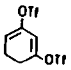
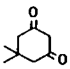
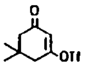
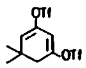
(*Received in UK* 3 *November* 1986)

Abstract.- Using 1,3-Cyclohexadione (1) and 5,5-dimethyl-1,3-Cyclohexadione (11) as examples, it is shown that 1,3-diketones can be transformed into monoketones, monoalcohols, alkanes and unsaturated ketones.

1,3-Diketones are an important class of compounds having a broad application in the field of organic synthesis[1]. They are normally prepared by intramolecular Claisen condensation of suitable ketoesters. One of their important synthetic uses is the preparation of cyclic and spirocyclic compounds by suitable transformation reactions[2-5]. As part of our programme in unveiling the potentialities of perfluoroalkanesulfonate esters[6] we disclose here our results on some interesting synthetic manipulations of 1,3-diketones via their vinyl triflates.

We chose the easily available 1,3-cyclohexadione (1) and 5,5-dimethyl-1,3-cyclohexadione (11) as sustrates, while they can offer an overview of the possibilities of the reactions carried out, - inspite of their symmetrical structure. Reaction of 1 with triflic anhydride in dimethoxyethane in the presence of sodium hydride at -78°C gave the mono-vinyl triflate 2. The bis-vinyl triflate 6 was prepared by treating 1 with an excess of triflic anhydride in the presence of 2,6-di-*tert*-buthyl-4-methylpyridine (DTMP) or sodium carbonate (Table 1) at room temperature for 12 h. Shorter reaction time led to a mixture of mono- and bis-vinyl triflates 2 and 6. The triflates 2 and 6 were found to be unstable in the pure form at room temperature and for this reason their - distillative purification was abandoned. However, they were isolated by column chromatography on silica gel and were found pure by gas chromatography and spectroscopical data.

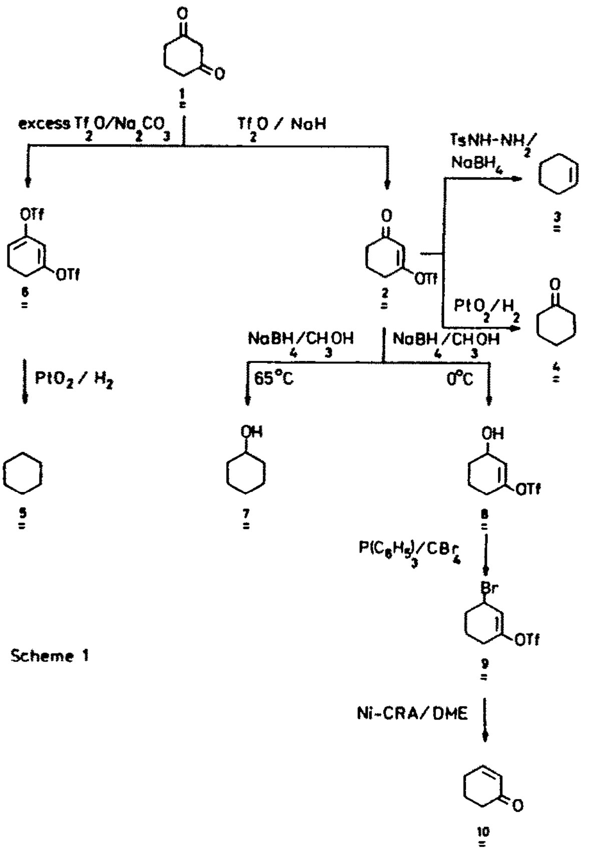
Table 1. Vinyl Triflates Prepared

Educt	Reagents/Solvent Temp (°C)/Time(h)	Product	Yield [a](%)
 1	Tf_2O,NaH/DME -78 /2	 2	87
1	Tf_2O,NaCO$_3$/CH$_2$Cl$_2$ r t. /12	 6	94
 11	Tf_2O,NaH/DME -78 /2	 12	80
11	Tf_2O,DTMP/CH$_2$Cl$_2$ r.t. /12	 13	77

---

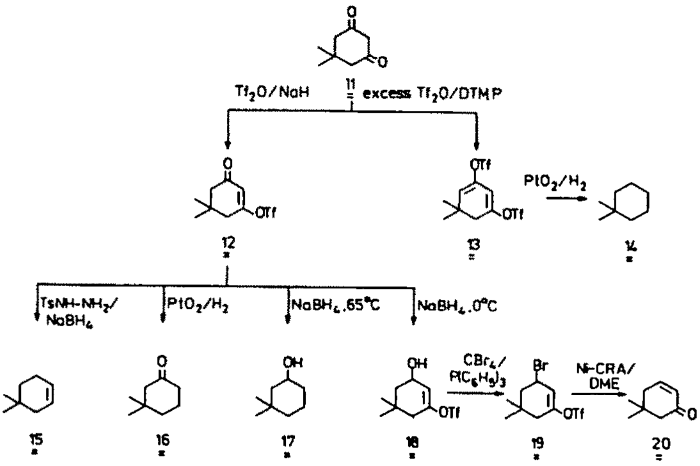
[a] Yield of isolated products. Purity ≥98% according GC.

Scheme 1 illustrates the reductive manipulation carried out on the triflates 2 and 6 (see also Table 2). While the bis-vinyl triflate 6 was completely hydrogenated to cyclohexane with hydrogen using PtO_2 as catalyst, the mono-vinyl triflate 2 was converted to an array of monofunctionalized derivatives 4, 7 and 10. The intermediate vinyl triflates 8 and 9 can also been used as interesting reactants in preparative organic chemistry[6].



Scheme 1

Analogous results were also obtained starting from 11 *via* the mono- and bis-vinyl triflates 12 and 13 respectively (Scheme 2).



Scheme 2

The conversion of **1** and **11** to **10** and **20** respectively were carried out via the hydroxy vinyltriflates **8** and **18**, by converting the latter to the bromo compound **9** and **19** with $CBr_4/P(C_6H_5)_3$ and sub-sequent reduction with the complex base Ni-CRA (NaH/t-AmOH/$Ni(OAc)_2$) in dimethoxyethane [7]. The yield of **10** and **20** from **8** and **18** were 35% and 43% respectively. The two-step reduction of 1,3-di-ketones **1** and **11** to the olefins **3** and **15** was achieved in an one-pot procedure by the reaction of ketones **2** and **12** with tosylhydrazine followed by reduction with sodium borohydride.

An example for the application of our method on the reduction to monoalcohols and monoketones has been carried out by us[8] on the unsymmetrical, sterically hindered 1,8,8-trimethylbicyclo [3.2.1] octa-2,4-dione.

Table 2. Reduction of Triflates

Educt	Reagent / Solvent Temp.(°C)/ Time(h)	Product No.	Yield[a] (%)	B.p. (°C)/torr	M.S. m/e(rel.Int.%)	IR(CCl_4) ν(cm^{-1})	^{1}H-N.M R.(CCl_4) δ(ppm)
2	PtO_2,H_2(1 Atm)/CH_3OH r.t. / 0.1	**4**	92	57-60/30[b]	98(M^+,50);70(30), 55(100);42(60) [b]		
12	PtO_2,H_2(1 Atm)/CH_3OH r.t. / 0.1	**16**	95	44-45/15[b]	126(M^+,34);111(20); 83(100);55(57) [b]		
2	$NaBH_4/CH_3OH$ 65 / 3	**7**	80	65-70/35[b]	100(M^+,2);82(54);67(36); 57(100);45(25) [b]		
2	$NaBH_4/CH_3OH$ 0 / 1	**8**	62	c	228(M^+-H_2O,45);95(228-Tf, 77);79(228-OTf,24);78(228- TfOH,40);67(100)	3440,1675,1420 1240,1140,1130	1.70(m,4H,CH_2);2.30(m,2H, $\underline{CH_2}$CHOH),2.60(s,1H,OH); 4.20(m,1H,C$\underline{H}$OH);5.70(m,1H, C=CH)
12	$NaBH_4/CH_3OH$ 65 / 3	**17**	83	66-68/14[b]	110(M^+-H_2O,33);95(100); 69(48);57(36) [b]		
12	$NaBH_4/CH_3OH$ 0 / 1	**18**	66	c	256(M^+-H_2O,21);123(256- Tf,24);95(76);91(100)	3350,1690,1420 1220,1140	1.05(d,6H,CH_3);1.50-2.00(m, 4H,CH_2);3 30(s,1H,OH);4.35(m,1H,C$\underline{H}$OH);5.70(m,1H,C=CH)
6	PtO_2,H_2(1 Atm)/CH_3OH r.t. / 1	**5**	60	81/760[b]	84(M^+,92);69(33), 56(100);55(32) [b]		
13	PtO_2,H_2(1 Atm)/CH_3OH	**14**	67	119/760[b]	112(M^+,25);97(100); 67(50);56(44); 55(77) [b]		

[a] Yield of isolated products

[b] Identified by comparison with an authentic sample

[c] Not determined due to descomposition

Table 3. Reaction Conditions and Products 3, 9, 10, 15, 19, 20 obtained [a]

Reactant	Reaction Conditions			Product	Yield	B.p.
	Reagent / Solvent	Time(h)	Temp.(°C)	No.	(%)	(°C)/torr
2	1. $TsNHNH_2$					
	2. $NaBH_4/CH_3OH$	11	65	**3**	42	81-82/760
8	$CBr_4/P(C_6H_5)_3$/ether	2	r.t.	**9**	52 [b]	---------
9	Ni-CRA/DME	1	r t.	**10**	35	40-45/30
12	1. $TsNHNH_2$					
	2. $NaBH_4/CH_3OH$	11	65	**15**	49	115-118/760
18	$CBr_4/P(C_6H_5)_3$/ether	2	r.t.	**19**	89 [b]	---------
19	Ni-CRA/DME	1	r.t.	**20**	43	88-89/32

[a] All the products are known and identified by comparison with an authentic sample as well as by their spectral data

[b] Crude yield

Experimental.

3-Trifluoromethylsulfonyloxycyclohex-2-en-1-one (2):

To a stirred mixture of sodium hydride (1.10 g, 45 mmol) in dimethoxyetane (125 ml) is added dropwise a solution of 1 or 11 (48 mmol) in dimethoxyetane (25 ml) at room temperature. After the evolution of hydrogen is over, the mixture is stirred for an additional 25 min, cooled to -78°C and triflic anhydride (12.4 g, 44 mmol) is added to it slowly. After stirring for 2 h at -78°C, the mixture is warmed to room temperature, the dimethoxyetane is removed under reduced pressure and the residue is taken up in dichloromethane (200 ml). The organic layer is washed with saturated sodium hydrogen carbonate (100 ml), water (100 ml), dried with magnesium sulfate and the solvent is removed under reduced pressure. The residue is chromatographed on a silica gel column (50 g) using chloroform as eluent (200 ml). Removal of solvent under reduced pressure affords spectroscopic and gas chromatographic (10% UCW 98, Chromosorb W-AW-DMCS, 80-100 mesh, 2 m x 1/4", 120°C) pure 2 or 12. Pure triflates can be stored in dilute *n*-pentane in the refrigerator.
U.V.(EtOH)λ:232 nm;logε:4.20 I.R.(CCl_4)ν:1685,1635,1430,1220,1140 cm^{-1}. ^{1}H-N.M.R.(CCl_4)δ:1.90-2.60 (m,6H,CH_2);5.90(m,1H,C=CH) ppm. M.S.m/e(%B):244(M^+,36);216(M^+-28,100);95(M^+-OTf,21).

5,5-Dimethyl-3-trifluoromethylsulfonyloxycyclohex-2-en-1-one (12):

U.V.(EtOH)λ:230 nm;logε:4.50 I.R.(CCl_4)ν:3070,1680,1645,1425,1215,1145 cm^{-1}. ^{1}H-N.M.R.(CCl_4)δ:1.10 (s,6H,CH_3);2.35(s,2H,CH_2CO);2.55(s,2H,CH_2C=C);5.95(s,1H,C=CH) ppm. M.S.m/e(%B):272(M^+,17);257(M^+-CH_3,6);244(M^+-28,13);216(M^+-C_4H_8,100).

1,3-Bistrifluoromethylsulfonyloxycyclohexa-1,3-diene (6):

To a stirred mixture of 1,3-Cyclohexadione (1, 2.70 g, 24 mmol) in dry dichloromethane (20 ml) containing anhydrous sodium carbonate (2.0 g) is added dropwise a solution of triflic anhydride (27.1g, 96 mmol) in dry dichloromethane (25 ml) at room temperature. The mixture is stirred for an additional 12 h, filtered and the organic layer is washed with saturated sodium hydrogen carbonate (100 ml) water (2x100 ml) and dried with sodium sulfate. Removal of solvent under reduced pressure and chromatography of the residue on silica gel (50 g) using *n*-hexane (250 ml) as eluent gives spectroscopically and GC pure 6; yield:8.5 g(94%). 6 can be stored in dilute *n*-pentane in the refrigerator.
U.V.(EtOH)λ:261 nm;logε:3.90 I.R.(CCl_4)ν:1670,1625,1425,1250,1150 cm^{-1}. ^{1}H-N.M.R.(CCl_4)δ:2.60(m,4H, CH_2);5.60-5.70(m,2H,C=CH) ppm. M.S.m/e(%B):376(M^+,32);243(M^+-Tf,27);93(243-TfOH,19);69(100).

5,5-Dimethyl-1,3-bis(trifluoromethylsulfonyloxy)-cyclohexa-1,3-diene (13):

To a stirred mixture of triflic anhydride (18.0 g, 64 mmol) and 2,6-di-*tert*-buthyl-4-methyl-pyridine[9] (5.6 g, 33 mmol) in dry dichloromethane (10 ml) is added a solution of 5,5-dimethylcyclohexa-1,3-dione (11, 4.2 g, 30 mmol) in dry dichloromethane (20 ml) at room temperature. The product is worked up as given under 6; yield:10.3 g(77%).
U.V.(EtOH)λ:261 nm;logε:3.90 I.R.(CCl_4)ν:1665,1620,1425,1250,1150 cm^{-1}. ^{1}H-N.M.R.(CCl_4)δ:1.20(s,6H, CH_3);2.50(s,2H,CH_2);5.45-5.80(s,2H,C=CH) ppm. M.S.m/e(%B):404(M^+,48);389(M^+-CH_3,41);271(M^+-Tf,18); 255(M^+-OTf,12);121(271-TfOH,44);69(100).

Hydrogenolysis of 2, 6, 12 and 13:

A mixture of the appropiate triflate (50 mmol) in absolute methanol (50 ml) containing Adam's-catalyst (PtO_2, 2% based on the substrate) is shaken in an atmosphere of hydrogen (1 bar) in a hydrogenation apparatus at room temperature. After the required amount of hydrogen is adsorbed, the catalyst is filtered, the solvent is removed under reduced pressure and the residue is diluted with water (100 ml) and extracted with dichloromethane (3x30 ml). The organic phase is dried with magnesium sulfate, the solvent is removed and the product is distilled (Table 2).

Cyclohexanol (7), 3,3-Dimethylcyclohexanol (17), 3-Trifluoromethylsulfonyloxycyclohex-2-en-1-ol (8), and 5,5-Dimethyl-3-trifluoromethylsulfonyloxycyclohex-2-en-1-ol (18):

To a solution of the appropiate vinyl triflate 2 or 12 (25 mmol) in methanol (40 ml) is added sodium borohydride (4.60 g, 120 mmol) in small portions. After the reaction is complete (Table 2), the solvent is evaporated under reduced pressure and the residue is taken up in ether (100 ml). The ether phase is washed with water (2x50 ml), 1N hydrochloric acid (2x50 ml), saturated sodium hydrogen carbonate solution (2x50 ml), water (2x50 ml) and dried with sodium sulfate. The solvent is removed under reduced pressure and the residue is distilled except in the cases of the triflates

8 and 18 (Table 2). Compounds 8 and 18 have been found to be unstable at room temperature and descompose partly during GC analysis.

3-Bromocyclohex-1-en-1-yl (9) and 3-Bromo-5,5-dimethylcyclohex-1-en-1-yl Triflate (19):

To a stirred solution of 8 or 18 (7 mmol) and carbontetrabromide (4.6 g, 15 mmol) in ether (40 ml) cooled to 0°C is added triphenylphosphine (3.6 g, 15 mmol). The mixture is stirred for an additional 2 h at room temperature, filtered and the filtrate concentrated under reduced pressure. The residue is extracted with n-pentane (3x30 ml), dried with magnesium sulfate and the solvent removed under reduced pressure. The tribromomethane formed is removed under vacuum at 0.1 torr at - room temperature (Table 3). Compounds 9 and 19 descompose quickly in pure form at room temperature, and therefore should be used immediately for the next step.

Cyclohex-2-en-1-one (10) and 5,5-Dimethylcyclohex-2-en-1-one (20):

To a stirred suspension of the complex NaH/t-AmOH/Ni(OAc)$_2$ (Ni-CRA)[7] (4.1 g, 10 mmol) in dime--thoxyethane (30 ml) is added a solution of 9 or 19 (10 mmol) in dimethoxyethane (15 ml) at room temperature. The solvent is removed under reduced pressure after 0.5 h and the residue is taken up in ether (100 ml). The ether phase is washed with 1N hydrochloric acid (2x50 ml), saturated sodium hydrogen carbonate (2x50 ml) and water (2x50 ml). The organic layer is dried with sodium sulfate, the solvent removed and the residue is distilled.

Cyclohexene (5) and 4,4-Dimethylcyclohexene (15):

A solution of the appropiate triflate 2 or 12 (10 mmol) and p-toluenesulfonylhydrazine (2.43 g, 13 mmol) in methanol (50 ml) is refluxed for 3 h. The mixture is cooled to room temperature and sodium borohydride (3.83 g, 10 mmol) is added in small portions to it and refluxed for 8 h. The methanol is removed under vacuum and the residue is dissolved in ether (100 ml). The ether layer is washed with water (2x50 ml), 1N hydrochloric acid (2x50 ml), saturated sodium hydrogen carbonate solution (2x50 ml), water (2x50 ml) and dried. Removal of solvent and distillation yields the product (Table 3).

Acknowledgement

We thank Stiftung Volkswagen-Werk for the financial support of this work.

References

1. Houben-Weyl, Methoden der Organischen Chemie, 4 th Edn., Vol. VII/2a-c, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, 1973, 1976 and 1977.
2. V. Gatah, N. N. Saha, P. C. Dutta, J. Am. Chem. Soc., 79, 4487 (1957).
3. W. Reusch in, Reduction, R. L. Agustine, Ed., Marcel Dekker, New York, 1968.
4. R. B. Woodward, E. Logusch, K. P. Nambiar, K. Sakan, D. E. Ward, J. Am. Chem. Soc., 103, 1981 (3210).
5. J. F. Ruppert, J. D. White, J. Am. Chem. Soc., 103, 1981 (1808).
6. P. J. Stang, M. Hanack, L. R. Subramanian, Synthesis, 82, 1982.
7. R. Vanderesse, J. J. Brunet, P. Caubere, J. Org. Chem., 46, 1981 (1270).
8. L. R. Subramanian, A. García Martínez, A. Herrera Fernández, R. Martínez Alvarez, Synthesis, 481, 1984.
9. P. J. Stang, W. Treptow, Synthesis, 283, 1980.