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PHOTOCHEMISTRY OF 6-TRIFLUOROMETHYL-2-CYCLOHEXENONE

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SUMMARY

The photochemical behaviour of the title compound, newly synthesized from 2-trifluoromethylcyclohexanone by a bromination/dehydrobromination sequence, is compared to that of 6-methyl-2-cyclohexenone. Both compounds behave similarly regarding photocyclodimerization and addition to 2-methylpropene. Higher yields of reduction (electron transfer) products from the trifluoromethyl- vs. the methyl enone are obtained in the irradiations in the presence of 2,3-dimethyl-2-butene or in 2-propanol, respectively.

INTRODUCTION

In previous papers we have described the photochemical behaviour of 2-trifluoromethylcyclohexanone (<u>1a</u>) [1], of other 2-(perfluoroalkyl)cycloalkanones [2], as well as that of 1,1,1-trifluoro-3-alkyn-2-ones [3]. The substitution of a CH_3 by a CF_3 group in such compounds had led to an enhanced formation of photoreduction products [4]. We now report comparative studies on light induced reactions of 6-trifluoromethyl-2-cyclohexenone (<u>2a</u>) and of the non-fluorinated enone <u>2b</u>.

RESULTS AND DISCUSSION

The previously unknown 6-trifluoromethyl-2-cyclohexenone (<u>2a</u>) was synthesized from 2-trifluoromethylcyclohexanone (<u>1a</u>) in two steps. Bromination of <u>1a</u> in CCl₄ affords trans-2-bromo-6-trifluoromethylcyclohexanone (<u>3</u>) in 70% yield. The configuration of <u>3</u> is proven by its ¹H-NMR spectrum, which shows the hydrogen on C(2) - adjacent to bromine - to be equatorial (two

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small vicinal coupling constants) and the hydrogen on C(6) to be axial. Treatment of <u>3</u> with CaCO₃ in dimethylacetamide [5] gives <u>2a</u> in 52% yield. 6-Methyl-2-cyclohexenone (<u>2b</u>) was obtained by dehydrogenation of 1-trimethylsilyloxy-2-methylcyclohexene (from 2;methylcyclohexanone <u>1b</u> and TMSiCl) with DDQ [6].



We first investigated relative rates of conversion for 2a and 2b on excitation (λ = 350 nm) under different reaction conditions. The results for 10⁻¹M solutions of 2a or 2b in (i) benzene (photocyclodimerization, formation of 4); (ii) in benzene saturated with 2-methylpropene or containing 1M 2,3-dimethyl-2-butene (photocycloaddition or photoaddition to an alkene, both types of products, e.g. 5 or 7, being formed from a common 1,4biradical intermediate); and (iii) 2-propanol (photoreduction, i.e. electron transfer to the excited enone followed by proton transfer and either coupling or disproportionation of the resulting radicals, with formation of e.g. 13 or 1, respectively), as compared to the rate of conversion of 10^{-1} M 2-cyclohexenone in benzene (relative rate = 1) under the same irradiation conditions are summarized in Table 1. It can be seen that both 2a and 2b undergo photodimerization slower than 2-cyclohexenone itself, most probably due to steric reasons, the CF_2 enone reacting about 20% faster than the methyl compound. In the three other reactions the figures for 2aare again all higher than the corresponding ones for 2b.

TABLE 1

Relative rates of conversion of $\underline{2a}$ or $\underline{2b}$ $(10^{-1}M)$ on excitation, as compared to 2-cyclohexenone $(10^{-1}M$ in benzene, k = 1.0)

	с ₆ н _б	C ₆ H ₆ saturated with 2-methylpropene	C ₆ H ₆ containing 1M 2,3-dimethyl-2-bute	2-propanol ne
<u>2a</u>	0.5	4.6	2.6	1.9
<u>2b</u>	0.4	3.3	1.4	1.5

The photodimerization of 2-cyclohexenones and related α , β -unsaturated carbonyl compounds has been thoroughly investigated [7-11]. Head-head (HH) and head-tail (HT) dimers arise due to the two possible orientations in the addition. The configuration of the two cycloalkanone rings fused to the cyclobutane ring can be either syn or anti, and the ring fusions are generally cis. From 2-cyclohexenone itself the HH-anti- and the HT-anti dimers are formed preferentially out of four possible products in a variety of solvents, the relative amount of the HH-dimer increasing with increasing solvent polarity [10-12]. The introduction of a substituent on C(6) of the 2-cyclohexenone gives rise to a much higher number of diastereomeric tricyclic dimers, as these substituents can occupy either axial or equatorial positions in the products. Indeed, irradiation of 2a in either benzene or acetonitrile gives mixtures of ten dimers 4aa - 4aj as analyzed by GC. The product distribution as well as their mass spectroscopic data are summarized in Table 2. In changing solvent from benzene to CH₂CN the relative amount of <u>4ad</u>, <u>4ag</u> and <u>4aj</u> increases while that of the other dimers decreases, suggesting the former to be HH-dimers and the latter HT-dimers. This assumption is supported by the fact that the mass spectra of these three dimers are very similar (type A) and distinctly different to those of 4ab, 4ae, 4af and 4ah on the one side (type B) and 4aa, 4ac and 4ai on the other side (type C). Further evidence comes from the isolation of 4aj by fractional crystallization, the analysis of its ¹H-NMR spectrum (Table 3) indicating an HH-anti-structure. Finally this same dimer 4aj was shown to split into antipodes on a chiral GC phase, as expected for a molecule of this configuration [10]. The HH-dimers 4ad, 4ag and 4aj - probably all of anti-configuration - make up for 25% of all dimers in C_6H_6 and for 58% in CH_3CN . The proposal of HT-anti structures for 4ab, 4ae, 4af and 4ah (59% in C_6H_6 vs. 36% in CH_3CN) and HT-syn structures for $\underline{4aa}$, $\underline{4ac}$ and $\underline{4ai}$ (16% in C_6H_6 vs. 6% in CH_3CN) is tentative, and based on the relative stabilities of such compounds. Under similar irradiation conditions 2b is known to afford a mixture of dimers 4b [7].



Dimer ^ć	1	с _б н _б	c	TH ₃ CN		MS	5	Structu
4aa		3.4		1.7		С		HT-syn
4ab		9.0	ŗ	5.8		В		HT-anti
4ac		3.9	:	2.4		C		HT-syn
4ad		9.4	15	5.5		A		HH-anti
<u>4ae</u>		27.3	20	0.0		в		HT-anti
4af		4.3	2	2.4		В		HT-anti
4ag		9.5	30	0.5		A		HH-anti
4ah		18.5		7.8		В		HT-anti
<u>4ai</u>		8.3		3.4		С		HT-syn
4aj		4.0	1	1.8		A		HH-anti
	m/e	328 (M [*])	232	218	165	91	80	68
A		15%	23%	_	27%	26%	70%	100%
в		48	-	20%	10%	10%	25%	100%
С		6%	-	-	20%	25%	100%	70%

Product distribution and mass spectroscopic data of photodimers 4a

a ordered as to their retention time on a SE 30 capillary GC column

Excited cyclic enones react with alkenes to afford photocycloaddition and photoaddition products [13, 14]. 2-Cyclohexenone itself gives trans-7, 7-dimethylbicyclo[4.2.0]octan-2-one (26%) and 2-(2'-methyl-2'-propenyl)cyclohexanone (14%) as major products with 2-methylpropene [15, 16]. The behaviour of <u>2a</u> and <u>2b</u> on irradiation in benzene solutions saturated with 2-methylpropene is found to be very similar. The four principal products - product distribution as determined by GC - are given below.



TABLE 2



Finally we investigated the photochemical behaviour of 2a and 2b in 2-propanol, a solvent wherein 2-cyclohexenone affords both tricyclic dimers and the 2H-reduction product (cyclohexanone) [17]. From 2a a 1:4:4 mixture of 1a, cis- and trans-2-trifluoromethyl-5-(1-hydroxy-1-methyl)ethylcyclohexanone is obtained selectively, whereas 2b affords similar products but in addition about 50% tricyclic dimers 4b.



The assignment of the structures of the photoproducts is based on their ¹H-NMR- (Table 3) and mass spectra (Table 4), the determination of their configuration and conformation emanating from the analysis of the signals of the hydrogens on the carbon atoms vicinal to the C=O group (H(2) and H(6), the former being the one next to CF₃). Although the chemical shift of H(2) (3.0 \pm 0.1 ppm) is more or less invariant, the differentiation between such an axial or equatorial H-atom - and therefore also of the CF₃ groups - is straightforward, as H_a(2) gives two large coupling constants with the two hydrogens on C(3) and, in rigid molecules, an additional long range coupling with H_a(6), wheras the coupling constants of H_e(2) with H_a(3) and H_e(3) are small. It is noteworthy that J_{HF} is larger for H_e(2) than for H_a(2) (11 vs. 8 Hz).

Irradiation of <u>2a</u> or <u>2b</u> in the presence of 2,3-dimethyl-2-butene also affords mixtures of cycloaddition and addition products, respectively:

TABLE	1
TABLE	

Compound	н(2) [С <u>н</u> Сг ₃]	н (6) [Снсо]	Others ^a
<u>4aj</u>	3.05 b,c	3.30 ^{b,d}	
<u>5a</u>	3.08 b,e	2.75 ^{b,f}	2.00 (dd, 11, 10)
<u>5b</u>	đ	2.80 ^{b,f}	1.65(dd, 10, 6.5)
<u>6a</u>	2.95 ^h ,i	2.90 ^{b,j}	
<u>6b</u>	g	2.90 ^{b,j}	
<u>7a</u>	3.05 ^{b,e}	2.50 ^k	2.60(da, 14.5, 4.5) ¹
<u>7b</u>	2.45 ^k	2.45 ^k	1.95(dd, 14.5, 10) 2.55(dd, 14.5, 4.5)
<u>8a</u>	3.05 ^{b,c}	2.50 j , 2.00 b	1.95(dd, 14.5, 10)
<u>8b</u>	g	g)	ĩ
<u>9a</u>	2.95 b,e	2.40 ^{b,m}	
<u>9b</u>	g	2.40 ^{b,m}	
<u>10a</u>	2.95 ^{h,i}	2.50 ^{b,n}	
<u>10b</u>	g	2.50 ^b ,n	
<u>11a</u>	2.80 b,c	2.85 ^{b,0}	
<u>12a</u>	3.05 ^{b,e}	2.40 ^{h,p} , 2.10 ^l	b,q 1
<u>13a</u>	3.05 ^{h,i}	$2.60^{h,r}$, 2.40^{l}	b,s
<u>14a</u>	3.05 ^{b,e}	2.60 ^h , ^p , 2.25 ^l	p,q

¹H-NMR spectroscopic data of photoproducts $\underline{4} - \underline{14}$

^a $H_{e}(3): 2.45 \text{ ppm}, \text{dddd}, J = 13, 5, 3, 2$ ^b axial proton ^c ddq, 13, 5, 8 ^d AA'XX' ($J_{AX} = 10, J_{AX'} = -1, J_{AA'} = 10, J_{XX'} = 3$) ^e dddq, 13, 5, 1, 8 ^f dddd, 13, 11, 6.5, 1 ^g chemical shift not determined ^h equatorial proton ⁱ ddq, 7, 3, 11 ^j ddd, 13, 11, 6 ^k coupling constants not determined ¹ 4.80 and 4.65 (s), 1.70 (s, 3H) ^m dd, 13.5, 1 ⁿ d, 13.5 ^o d, 9.5 ^p ddd, 13, 5, 3 ^q dt, 1, 13 ^r dd, 13, 3 ^s t, 13.

Mass spectroscopic data of photoproducts 5 -14

Compound		l	ŧ	0.11
conpound		Base peak	<u> </u>	Others
<u>5a</u> and <u>6a</u>	220 (14%)	82 ^a	30%	165 (35%) ^b
<u>5b</u> and <u>6b</u>	166 (33%)	111 ^b	-	
<u>7a</u>	220 (28%)	95 ^C	23%	67 (67%) ^d
<u>7</u> b	166 (29%)	67 ^d	-	95 (75%) ^C
<u>8a</u>	220 (3%)	165 ^b	13%	
<u>8b</u>	166 (7%)	55	-	111 (73%) ^b
<u>9a</u> and <u>10a</u>	248 (2%)	82 ^a	13%	
9b and <u>10b</u>	194 (3%)	83 ^e	-	
<u>11a</u>	248 (2%)	82 ^e	18%	
<u>12a</u>	248 (0.1%)	83 ^e	88	
<u>13a</u> and <u>14a</u>	224 (0.1%)	59 ^f	18%	

^a
$$(CH_3)_2C=CH-CH-CH_2^*$$

^b [enone + H]^{*}
^c $CH_2=C(CH_3)CH=CH-C=O^*$
^d 95 - co
^e $CH_2=C(CH_3)C(CH_3)_2^*$
^f $(CH_3)_2COH^*$

The six- and the four membered ring in the bicyclo[4.2.0] ∞ tan-2-ones are generally trans-fused ($J_{H_a(6),H_a(5)} = 13$ Hz), the minor cycloadduct <u>11a</u> (10% from <u>2a</u> and 2,3-dimethyl-2-butene) representing the only exception. The position of the 2-methyl-2-propenyl side chain in compounds <u>7</u> (on C(6)) and <u>8</u> (on C(5) becomes evident by comparison of the ¹H-NMR spectra of <u>7</u> with those of 2-halogeno-6-alkyl-2-cyclohexanones reported in the literature [18]. Only when this side chain is located on C(6) is the signal of one of the two hydrogen atoms on C(1') shifted to lower field (2.6 ppm) due to the anisotropy of the C=O group. In the mass spectra of compounds 7 the signal at m/e = 95, corresponding to the fragment $CH_2=C(CH_3)CH=CH-C=0^+$, formed by elimination of either ethylene, H and 1,1,1-trifluoropropene (from <u>7a</u>) or ethylene, H and propene (from <u>7b</u>), is very intensive, proving the chain to be located on C(6) of the cyclohexanone ring. For compounds <u>12a</u>, <u>13a</u> and <u>14a</u> the chemical shifts and coupling constants fully correspond to those reported for alkylated 2-chlorocyclohexanones [19, 20].

Increased formation of reduction products from excited $\underline{2a} \text{ vs. } \underline{2b}$ is to be expected, given the difference of about 200 mV in their reduction potentials $(E_p \text{ vs. } \text{Ag/Ag}^+ (10^{-1}\text{M}) \text{ in CH}_3\text{CN} \text{ with } 0.5\text{M Bu}_4\text{N}^+\text{Clo}_4^-$ as electrolyte, $\underline{2a}$: -2.22V, $\underline{2b}$: -2.43 V). This is indeed observed in 2-propanol, where $\underline{2b}$ affords 50% reduction products and 50% dimers whereas $\underline{2a}$ gives reduction products selectively, as well as in the formation of a 5-(1,1,2-trimethyl-2-propenyl)cyclohexanone with 2,3-dimethyl-2-butene only from $\underline{2a} (\underline{12a}, 20\%)$. These RH-reduction products $\underline{12} - \underline{14}$ are formed via electron transfer to the excited enone , followed by proton transfer in the radical ion pair and coupling of the resulting radicals [3, 4]. The fact that no such differential behaviour between $\underline{2a}$ and $\underline{2b}$ is observed in their reactions with 2-methylpropene, where from both enones only minor amounts of $\underline{8}$ are formed, is most probably due to the higher ionisation potential of this alkene as compared to that of 2,3-dimethyl-2-butene.

$$\underline{2^*} + RH \longrightarrow \mathbb{C}^{\bullet} + RH^{\ddagger} \longrightarrow \mathbb{C}^{\bullet} + R^{\ddagger} \longrightarrow \mathbb{C}^{\bullet} + R^{\ddagger} \longrightarrow \mathbb{C}^{\bullet}$$

EXPERIMENTAL

General

Chemical shifts in the 400-MHz 1 H-NMR spectra are given in ppm relative to TMS (coupling constants J in Hz). Mass spectra were recorded at 70 eV. Analytical GC was performed on a SE 30 capillary column. Preparative GC separations were run on 2m 25% Carbowax 20M (column <u>A</u>) or 2m 10% QF1 (column <u>B</u>).

Starting Materials

6-Methyl-2-cyclohexenone (<u>2b</u>) [6] was synthesized according to the literature. 2-Methylpropene and 2,3-dimethyl-2-butene were purchased from FLUKA AG.

(a) Preparation of trans-2-bromo-6-trifluoromethylcyclohexanone (3)

To a solution of 3.9 g 2-trifluoromethylcyclohexanone (<u>1a</u>) [1] in 100 ml CCl₄ at 0° is added a solution of 4.5 g bromine in 50 ml CCl₄. After stirring for 2h at 0° and 12h at r.t. the solvent is evaporated and the residue distilled to afford 4.3 g (76%) <u>3</u>, b.p. 98-103°/14 mm. ¹H-NMR (CDCl₃): 4.45 (t, J = 3 Hz), 3.95 (ddg, J = 13, 5.5, 8 Hz), 2.4 - 1.7 (m, 6H). ¹³C-NMR (CDCl₃): 196, 125 (q, J = 273 Hz), 52, 48 (q, J = 26 Hz), 35, 27, 19. MS: 246 + 244 (M⁺, 13%), 41 (C₃H⁺₅, 100%).

(b) Preparation of 6-trifluoromethyl-2-cyclohexenone (2a)

A mixture of 3.8 g $\underline{3}$ and 12.5 g CaCO₃ in 80 ml dimethylacetamide is stirred at 130° for 15h. 500 ml Water are added and the solution extracted three times with 25 ml ether. The organic phase is washed twice with saturated NaCl solution and dried over MgSO₄: After evaporation of the solvent the residue is chromatographed (SiO₂, CH₂Cl₂) to afford 1.5 g (58%) <u>2a</u>. ¹H-NMR (CDCl₃): 7.05 (dt, J = 10, 1 Hz), 6.10 (dt, J = 10, 2 Hz), 3.08 (ddg, J = 11, 5, 8), 2.6 - 2.1 (m, 4H). ¹³C-NMR (CDCl₃): 191, 151, 130, 125 (q, J = 280 Hz), 50 (q, J = 25 Hz), 24, 23. MS: 164 (M⁺, 24%), 68 (CH₂=CH-CH=C=O⁺, 100%).

Photolyses

These were performed in a Rayonet RPR-100 photoreactor using 350 nm lamps. Argon-degassed solutions of 164 mg $\underline{2a}$ or 110 mg $\underline{2b}$ (10⁻³ mol) in 10 ml of either benzene, 2-propanol or acetonitrile, benzene saturated with 2-methylpropene or containing 840 mg (10⁻² mol) 2,3-dimethyl-2-butene were irradiated for 24 - 70h (monitoring by GC). With the exception of dimer $\underline{4aj}$, obtained by fractional crystallization, all products were isolated by prep. GC as liquids or oils.

Irradiation of 2a

(a) In benzene

Irradiation period: 70h. All attempts to isolate pure dimers 4a by either chromatography or fractional crystallization were unsuccessful.

(b) In acetonitrile

Irradiation period as above. Evaporation of the solvent dissolving the residue in 1 ml $CHCl_3/CCl_4$ 1:1 and cooling to -5° affords 10 mg (6%) of crystalline <u>4aj</u>, m.p. 185° (dec.).

(c) In benzene saturated with 2-methylpropene

Irradiation period: 21h. After evaporation of the solvent preparative GC on column <u>B</u> (isotherm. 140°) affords four fractions, first <u>6a</u> (60% purity), second 7a (85% purity), third 8a (95% purity) and finally 5a (97% purity).

(d) With 2,3-dimethyl-2-butene

Irradiation period as under (c). Separation on column <u>A</u> (isotherm. 170°) affords four fractions of greater 90% purity, first <u>10a</u>, second <u>11a</u>, third <u>9a</u> and finally <u>12a</u>.

(e) In 2-propanol

Irradiation period as under (c). Separation on column <u>B</u> 80 - 200°, 5°/min affords three fractions of greater 95% purity, first <u>1a</u>, second <u>13a</u> and finally <u>14a</u>. Compound <u>13a</u> isomerizes to <u>14a</u> on standing at r.t. in 5-7 days, or in 5 min. on contact with basic alumina.

Irradiation of 2b

(a) With 2-methylpropene

Irradiation period: 20h. Separation on column <u>A</u> (90 - 130°, 5°/min) affords three fractions of greater 80% purity, first <u>7b</u>, second a 1:1 mixture of <u>5b</u> and <u>6b</u> and finally 8b.

(b) With 2,3-dimethyl-2-butene

Irradiation period as above. Separation on column <u>A</u> (isotherm. 140°) affords one fraction, a 1:1 mixture of <u>9b</u> and <u>10b</u>, of 90% purity.

(c) In 2-propanol

Irradiation period as above. The mixture was analyzed by GC/MS

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