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Synthesis of αβ-Unsaturated Trifluoromethyl Ketones from 4-Dimethylamino-1,1,1-trifluorobut-3-ene-2-one by Addition of Grignard Reagents

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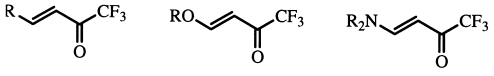
Abstract—Enaminones are available by reaction of 4-ethoxy-1,1,1-trifluorobut-3-ene-2-one with amines such as dimethylamine and they react with Grignard reagents to give αβ-unsaturated trifluoromethyl ketones in good yield by 1,4-addition followed by elimination. The generality of this procedure is contrasted with reactions based either on the use of organolithium nucleophiles, or the use of 4-alkoxy-αβ-unsaturated trifluoromethyl ketones as electrophilic partners.

Introduction

The present strongly developed interest[1] in organofluorine chemistry, and particularly the construction of simple fluorine building blocks appropriate for subsequent synthetic elaboration, has led to considerable study of, in general, trifluoromethylketones[2] and, in particular, α,β-unsaturated[3–11] trifluoromethylketones (**1**). Such ketones have been used as intermediates in heterocyclic synthesis[12] and have also been viewed as synthetic targets[13] because of their possible pharmacological interest. Whilst trifluoromethyl ketones constitute a particularly well documented class of serine protease inhibitors which have proven attractive against elastase, chymotrypsin and CMV protease[14] and aromatic trifluoromethyl ketones are found to be inhibitors of *helicobacter pylori*,[15] the published routes to such α,β-unsaturated trifluoromethylketones (**1**) are fraught with difficulties. These are highlighted by the comments, methods for the synthesis of trifluoromethyl ketones are scarce[16] and in reference to the most developed route of nucleophilic trifluoromethylation of esters, there were until recently few reports of successful synthetic methodology.[17] Some routes[3] require organofluorine reagents less readily available than trifluoroacetic anhydride and other routes[5] are multi-step. Aldol condensation[8] of trifluoromethylketones with aldehydes is inefficient. An earlier route[9] depends upon the addition of vinyl Grignard reagents to trifluoroacetic acid and proceeds in low yield. Two potentially promising routes are the use of organometallic reagents in additions to acetylenic trifluoromethylketones and in additions to β-substituted-αβ-unsaturated ketones, such as the ketones (**2**) and (**3**). Organocuprate additions to acetylenic trifluoromethylketones afford[7] products by both 1,2- and 1,4-addition. Again organometallic additions to β-substituted unsaturated trifluoromethyl ketones (**2**) and (**3**) might lead to products of 1,2- or 1,4-addition. A well investigated route with non-fluorinated analogues has concerned the displacement of alkoxy groups. The ketones (**2**) are readily available by acylation of the alkylvinyl ethers with trifluoroacetic anhydride, but the value of this route is limited. Reaction[6] of phenylmagnesium bromide with the ketone (**2**, R=Et) at 0°C gives an unsaturated ketone, a product of 1,2-addition, in only 20–30% yield. Side reactions by direct attack at the carbonyl group occur. Similarly additions of organozinc reagents to the ketones (**2**) are complicated by the dominance of 1,2-addition giving undesired products. Addition elimination sequences based on β-halo- or β-alkylthio- analogues have been investigated, but not developed for the synthesis of unsaturated trifluoromethyl ketones.



(**1**) (**2**) (**3**)

An alternative route using the readily available[18–20] 4-dialkylamino-αβ-unsaturated ketones (**3**) has recently been studied. With non-fluorinated analogues of (**3**) some success has been achieved in such addition elimination reactions using not only Grignard,[21,22] organolithium[23] and organocuprate[24] reagents, but more recently[25] with organocerium reagents. In the synthesis of α,β-unsaturated

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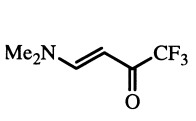
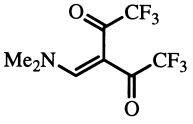
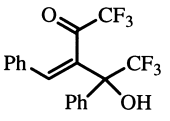
trifluoromethylketones (**1**) Balenkova et al.[11] have recently shown that aryllithiums add to the 4-dimethylamino-αβ-unsaturated trifluoromethylketone (**4**) by 1,4-addition. In contrast in the one reported example using a Grignard reagent the diketone (**5**) was transformed[11] to the hydroxyketone (**6**) in only 18% yield. There are other reports of the contrasting behaviour of Grignard reagents and organolithium reagents with β-substituted-αβ-unsaturated ketones. In a recent study[21] with β-dialkylamino-αβ-unsaturated ketones although alkyllithiums undergo 1,4-addition, 1,2-addition is observed with Grignard reagents. There is a single example,[6] albeit in moderate yield, of 1,4-addition of a Grignard reagent to a β-dialkylamino-αβ-unsaturated trifluoromethylketone (**3**). With non-fluorinated analogues 1,4-additions of Grignard reagents[22] are well described. Not only is the distinction in the regiochemistry of additions to methyl- and trifluoromethylketones unclear, but the contrasting 1,4-addition of phenyl magnesium bromide to acyclic β-alkoxy-αβ-unsaturated ketones and the preferential 1,2-addition of the same reagent to cyclic β-alkoxy-αβ-unsaturated ketones, indicates that the expected outcome of Grignard additions to ketones such as (**2**) and (**3**) is unclear. In the light of our studies[26,27] with the readily available β-alkoxy- and β-dialkyl-dialkylamino-αβ-unsaturated trifluoromethylketones (**3**), we considered that reaction with a variety of Grignard reagents might provide a route to β-aryl-αβ-unsaturated trifluoromethylketones and β-alkyl-αβ-unsaturated trifluoromethylketones (**1**). In this paper we establish such procedures based both on Grignard and organolithium reagents.



(**4**)



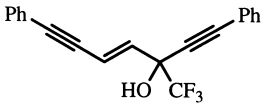
(**5**)



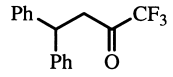
(**6**)

Results and Discussion

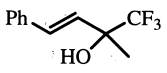
Reaction of enaminone (**4**) with the Grignard reagent prepared from 1-bromooctane and chromatographic purification gave the ketone (**7**) in 67% yield (see Table 1). In contrast to the analogous addition to the alkoxy analogues reaction is highly selective. Only 1,4-addition is observed and neither 1,2-addition products, nor products of further addition are isolated when 2 equiv. or less of Grignard reagent are used. Formation of the product (**7**) is also stereoselective. No *cis* product is observed. In a similar manner 1-bromoundecane and 1-bromododecane gave the ketones (**8**) and (**9**) respectively. Reaction is also efficient with Grignards derived from aryl halides. Bromobenzene, p-bromoanisole, 1-bromo-4-fluorobenzene, 3-bromotoluene and 1-bromonaphthalene gave the ketones (**10**), (**11**), (**12**), (**13**), and (**14**) respectively. Acetylenic Grignard reagents also react, but in contrast to those cases of addition of alkyl and aryl Grignard reagents where no reaction at the carbonyl centre is observed using 2 equiv. of a Grignard reagent, overreaction with phenylacetylenic magnesium bromide gave the alcohol (**15**) in addition to the expected ketone (**16**). An interesting difference was observed in the products of overaddition. With an excess of phenyl magnesium bromide, greater than 2 equiv., the product of further reaction was observed to be the ketone (**17**). In contrast the product of further reaction of methyl magnesium bromide with the ketone (**10**) was the alcohol (**18**). To illustrate the reaction of Grignard reagents derived from terminal alkylacetylenes, the Grignard derived from 1-decyne was reacted. A small amount of further reaction to afford the alcohol (**19**) was observed, but the unsaturated ketone (**20**) was obtained in 61% yield.



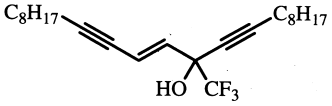
(**15**)



(**17**)



(**18**)

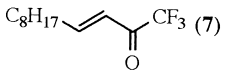
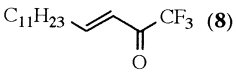
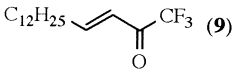
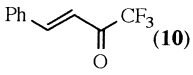
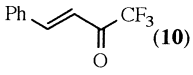
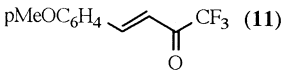
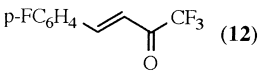
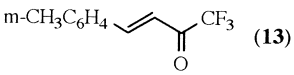
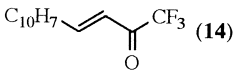
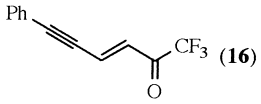
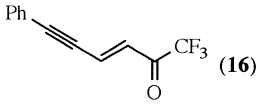
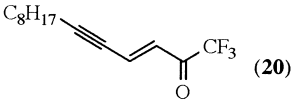


(**19**)

The addition of organometallic reagents other than Grignard reagents was briefly examined. A procedure using cerium(III) chloride, previously developed[25] with non-fluorinated enaminoketones, was examined. Using phenylmagnesium bromide we find that reaction with the enaminoketone (**4**) in the presence of $CeCl_3$ gives the unsaturated ketone (**10**), but with no enhancement of yield relative to the use of phenylmagnesium bromide alone. The reaction of ethyl bromoacetate with the enaminone (**4**), under Reformatsky conditions using zinc failed. However reaction with organolithium reagents is effective, but has no advantage over the addition of organomagnesium reagents. In the recent study of the addition of aryllithiums to the 4-dimethylamino-trifluoromethylketone (**4**) and to the dione (**5**) Balenkova et al.[11] report that reaction of butyllithium, in both cases, affords complex mixtures, and the expected products, unsaturated trifluoromethyl ketones could not be isolated. We find that reaction of 4-dimethylamino-trifluoromethylketone (**4**) with phenyl lithium afforded the ketone (**10**) in 42% yield and the lithium derivative of phenylacetylene gave the ketone (**16**) in 37% yield. By contrast with these examples, our results shown in Table 1 of reactions with a variety of magnesium reagents derived from alkyl- and aryl-derivatives, establish the preference in preparation of unsaturated trifluoromethyl ketones of the use of Grignard reagents.

In the two accompanying papers[26,27] we show that the 4-dialkylamino-αβ-unsaturated trifluoromethylketones (**3**) are less reactive than the analogous 4-alkoxy-αβ-unsaturated trifluoromethylketones (**2**). We describe cases where it is necessary to use the latter with less reactive nucleophiles in order to achieve satisfactory transformations. In contrast with more reactive organometallic nucleophiles there is merit in matching less reactive partners. Thus in

Table 1. Synthesis of unsaturated trifluoromethyl ketones

Enaminone substrate	Nucleophile	Product	Yields (%)
(**4**)	*n*-$C_8H_{17}MgBr$	 (**7**)	67
(**4**)	*n*-$C_{11}H_{21}MgBr$	 (**8**)	60
(**4**)	*n*-$C_{12}H_{25}MgBr$	 (**9**)	38
(**4**)	PhMgBr	 (**10**)	47[a]
(**4**)	PhLi	 (**10**)	42
(**4**)	*p*-$MeOC_6H_4MgBr$	 (**11**)	58
(**4**)	*p*-FC_6H_4MgBr	 (**12**)	50
(**4**)	*m*-$CH_3C_6H_4MgBr$	 (**13**)	62
(**4**)	α-Naphthyl magnesium bromide	 (**14**)	80
(**4**)	PhCCMgBr	 (**16**)	37[a]
(**4**)	PhCCLi	 (**16**)	37
(**4**)	$C_8H_{17}CCMgBr$	 (**20**)	61[a]

[a] See text for additional products.

reaction of 4-dialkylamino-αβ-unsaturated trifluoromethylketones (**3**) and 4-alkoxy-αβ-unsaturated trifluoromethylketones (**2**) with aryllithium nucleophiles the less reactive 4-dialkylamino-αβ-unsaturated trifluoromethylketones (**3**) can be used more effectively. However instead of using the more reactive alkyllithiums with 4-dialkylamino-αβ-unsaturated trifluoromethylketones (**3**) there is preference for using organomagnesium reagents in transformations to give various αβ-unsaturated trifluoromethyl ketones. In particular such a strategy avoids the complications found in reactions of the 4-alkoxy-αβ-unsaturated trifluoromethylketones (**2**), where undesired side-products complicate the 1,4-mode of addition. In view of the current interest in trifluoromethyl ketones the methodology developed in this paper based on cheap readily available starting materials is likely to have many applications.

Experimental

General experimental methods are described in the previous paper.[27]

General procedure for the synthesis of trifluoromethylated α,β-unsaturated ketones (1)

A solution of the alkyl magnesium bromide was prepared from the corresponding alkyl (aryl) bromide (2.4–3.0 mmol) and dry magnesium turnings (2.4–3.0 mmol) in anhydrous diethyl ether (1.0 ml) by dropwise addition of the alkyl (aryl) halide followed by gentle heating until all the magnesium was consumed. A solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.20 g, 1.2 mmol) in anhydrous ether (6 ml) was then added to the solution of

the Grignard reagent at room temperature with stirring. The resulting mixture was heated under reflux for 2 h before the cold reaction mixture was poured into ice cold 2 M hydrochloric acid (14.5 ml). The ether layer was separated and the aqueous layer further extracted with ether (2×12 ml). The combined ether phases were washed with water (12 ml), dried over Na_2SO_4 and the solvent removed in vacuo. The crude product was purified by column chromatography (silica gel, neat petroleum ether) to afford the appropriate trifluoro substituted unsaturated ketone.

1,1,1-Trifluoro-3-dodecen-2-one (7). The Grignard reagent from 1-bromooctane (0.46 g) and magnesium (0.06 g) afforded as a colourless oil in 67% yield the known[5] 1,1,1-trifluoro-3-dodecen-2-one (**7**) (0.19 g) δ_H 7.34 (1H, dt J=15.8, 7.0 Hz, H-4), 6.41 (1H, dd J=15.8 Hz, 1.1, H-3), 2.34 (2H, dq J=1.5, 7.0 Hz, H-5), 1.52 (2H, m, H-6), 1.28 (s, 10H), 0.89 (3H, t J=6.6 Hz, H-12); δ_C 14.18 (C-12), 22.76 (C-11), 27.74 (C-10), 29.27 (C-8, C-9), 29.40 (C-7), 31.93 (C-6), 33.40 (C-5), 116.38 (q, C-1), 121.48 (C-3), 157.10 (C-4), 179.92 (q, C-2); δ_F −84.29 (CF_3); ν_{max} 2929, 2858, 1731, 1711 and 1628 cm^{-1}.

1,1,1-Trifluoro-3-pentadecen-2-one (8). The Grignard reagent from 1-bromoundecane (0.56 g) and magnesium (0.06 g) afforded as a colourless oil in 60% yield 1,1,1-trifluoro-3-pentadecen-2-one (**8**) (0.20 g) δ_H 7.34 (1H, dt J=15.8 Hz, 7.0, H-4), 6.41 (1H, dd J=15.8, 0.7 Hz, H-3), 2.34 (2H, dq J=1.4, 7.0 Hz, H-5), 1.52 (2H, m, H-6), 1.27 (s, 16H), 0.88 (3H, t J=6.6 Hz, H-15); δ_C 14.21 (C-15), 22.82 (C-14), 27.75 (C-13), 29.29 (C-12), 29.46 (C-11, C-10), 29.60 (C-9), 29.73 (C-7, C-8), 32.04 (C-6), 33.40 (C-5), 116.38 (q, C-1), 121.48 (C-3), 157.10 (C-4), 179.92 (q, C-2); δ_F −84.27 (CF_3); ν_{max} 2926, 2854, 1730, 1710 and 1628 cm^{-1}; found M^+ 278.1895. $C_{15}H_{25}F_3O$ requires M^+ 278.1858 *m/z* 278 (12), 249 (3), 235 (3), 221 (4), 209 (88), 179 (17), 165 (22), 97 (47), 69 (61) and 43 (100).

1,1,1-Trifluoro-3-hexadecen-2-one (9). The Grignard reagent from 1-bromododecane (0.60 g) and magnesium (0.06 g) afforded as a colourless oil in 38% yield the known[5] 1,1,1-trifluoro-3-hexadecen-2-one (**9**) (0.13 g) δ_H 7.34 (1H, dt J=15.8, 7.2 Hz, H-4), 6.41 (1H, dd J=15.8, 1.1 Hz, H-3), 2.33 (2H, dq J=1.5, 7.2 Hz, H-5), 1.52 (2H, m, H-6), 1.26 (s, 18H), 0.88 (3H, t J=6.8 Hz, H-16); δ_C 14.21 (C-16), 22.82 (C-15), 27.74 (C-14), 29.29 (C-13), 29.45 (C-12), 29.47 (C-11), 29.68 (C-10), 29.73 (C-9), 29.76 (C-7, C-8), 32.05 (C-6), 33.40 (C-5), 116.38 (q, C-1), 121.47 (C-3), 157.08 (C-4), 179.91 (q, C-2); δ_F −84.23 (CF_3); ν_{max} 2926, 2855, 1730, 1711 and 1629 cm^{-1}.

4-Phenyl-1,1,1-trifluoro-3-buten-2-one (10). The Grignard reagent from bromobenzene (0.38 g) and magnesium (0.06 g) afforded as a yellow oil in 47% yield the known[28] 4-phenyl-1,1,1-trifluoro-3-buten-2-one (**10**) (0.34 g) δ_H 7.98 (1H, d J=15.8 Hz, H-4), 7.57 (5H, m, phenyl), 7.03 (1H, dq J=15.8, 0.7 Hz, H-3), δ_C 116.55 (q, C-1), 116.76 (C-3), 129.39, 132.49, 133.46, 141.41 (phenyl), 150.31 (C-4), 180.16 (q, C-2); δ_F −84.23 (CF_3); ν_{max} 3065, 3031, 1720, 1610 and 1576 cm^{-1}.

4-(4-Methoxyphenyl)-1,1,1-trifluoro-3-buten-2-one (11). The Grignard reagent from p-bromoanisole (0.45 g) and magnesium (0.06 g) afforded as a yellow oil in 80% yield the known 4-(4-methoxyphenyl)-1,1,1-trifluoro-3-buten-2-one (**11**). Flash chromatography (eluant petroleum ether) and recrystallisation (ethanol) afforded in 58% yield the known[28] title compound as yellow crystals, (0.16 g) mp 47–48°C (lit. mp 38°C) δ_H 7.93 (1H, d J=15.8 Hz, H-4), 7.0 (2H, dd, J=6.6, 1.8 Hz, H-2′), 6.95 (2H, dd J=7.0, 1.8 Hz, H-3′, H-5′), 6.88 (1H, dd J=15.8, 0.7, H-3), 3.87 (3H, s, OCH_3); δ_C 55.66 (OCH_3), 114.17 (C-3), 114.90 (C-3′, C-5′), 116.33 (q, C-1), 126.31 (C-1′), 131.56 (C-2, C-6′), 150.13 (C-4), 163.34 (C-4′), 180.06 (q, C-2); δ_F −84.34 (CF_3); ν_{max} 3012, 2937, 2841, 1704, 1590 and 1568 cm^{-1}.

4-(4-Fluorophenyl)-1,1,1-trifluoro-3-buten-2-one (12). The Grignard reagent from 1-bromo-4-fluorobenzene (0.52 g) and magnesium (0.07 g) afforded in 50% yield the known[29] 4-(4-fluorophenyl)-1,1,1-trifluoro-3-buten-2-one (**12**) as white crystals (0.13 g) mp 39–41°C (ethanol-water) δ_H 7.94 (1H, d J=15.8 Hz, H-4), 7.66 (2H, dd, J=8.8, 5.1, 1.8 Hz, H-2′, H-6′), 7.15 (2H, dt J=8.5, 8.5, 1.8 Hz, H-3′, H-5′), 6.95 (1H, d J=15.8 Hz, H-3); δ_C 116.50 (q, C-1), 116.46 (C-3), 116.72 (d C-3′, C-5′), 129.80 (d, C-1′), 131.54 (C-2′, C-6′), 148.87 (C-4), 165.25 (d, C-4′), 180.01 (q, C-2); δ_F −84.16 (CF_3), −56.20 (ArF); ν_{max} 1716, 1613 and 1589 cm^{-1}; found M^+ 218.0350. $C_{10}H_6F_4O$ requires M^+ 218.0355 *m/z* 218 (51), 149 (100), 121 (44) and 97 (36).

4-(3-Tolyl)-1,1,1-trifluoro-3-buten-2-one (13). The Grignard reagent from 3-bromotoluene (0.51 g) and magnesium (0.07 g) afforded as a yellow oil in 62% yield 4-(3-tolyl)-1,1,1-trifluoro-3-buten-2-one (**13**) (0.16 g) δ_H 7.94 (1H, d J=15.8 Hz, H-4), 7.44–7.30 (4H, m, aromatic), 7.00 (1H, dd J=15.8, 0.7 Hz, H-3), 2.40 (3H, s, CH_3); δ_C 21.38 (CH_3), 116.55 (C-3), 116.57 (q, C-1), 126.72 (C-6′), 129.27 (C-4′), 129.93 (C-5′), 133.40 (C-2′), 139.19 (C-1′, C-3′), 150.57 (C-4), 180.17 (q, C-2); δ_F −84.28 (CF_3); ν_{max} 3030, 2926,1717, 1609 and 1583 cm^{-1}; found M^+ 214.0611. $C_{11}H_9F_3O$ requires M^+ 214.0605 *m/z* 214 (79), 199 (56) and 145 (100).

4-(1-Naphthyl)-1,1,1-trifluoro-3-buten-2-one (14). The Grignard reagent from 1-bromonaphthalene (0.50 g) and magnesium (0.06 g) afforded as a yellow oil in 80% yield 4-(1-naphthyl-1,1,1-trifluoro-3-buten-2-one (**14**) (0.24 g) δ_H 8.80 (1H, d J=15.8 Hz, H-4), 8.14 (1H, d J=8.5 Hz, H-2′), 7.95 (1H, d J=7.5 Hz, H-4′), 7.87 (1H, d J=6.6, H-5′), 7.86 (1H, d J=8.0, H-8′), 7.59 (1H, dt J=7.5 Hz, 1.5, H-3′), 7.56 (1H, dt J=8.1, 1.1 Hz, H-6′), 7.48 (1H, dt, J=8.0, 1.1 Hz, H-7′), 7.10 (1H, d J=15.8 Hz, H-3), δ_C 116.70 (q, C-1), 118.65 (C-3), 122.96, 125.55, 126.24, 126.81, 127.82, 129.19, 130.47, 131.94, 132.98, 133.93 (naphthyl), 146.83 (C-4), 180.06 (q, C-2); δ_F −84.32 (CF_3); ν_{max} 3059, 2928, 1715, 1604 and 1570 cm^{-1}; found M^+ 250.0590. $C_{14}H_9F_3O$ requires M^+ 250.0605 *m/z* 250 (79), 181 (100), 153 (51), 127 (7) and 76 (27).

6-Phenyl-1,1,1-trifluoro-3-hexen-5-yne-2-one (16) and 1,7-diphenyl-3-hydroxy-3-trifluoromethyl-4-hepten-1,6-diyne (15). A solution of phenylacetylenic magnesium bromide was prepared from phenylacetylene (0.24 g) in anhydrous diethyl ether (4.0 ml) and 3 M ethylmagnesium

bromide in diethyl ether (0.80 ml) under nitrogen. A solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.20 g) in anhydrous diethyl ether (3.0 ml) was then added to the stirred solution of the Grignard reagent at room temperature. The resulting mixture was heated under reflux for 2.5 h, and after cooling was poured into ice cold 2 M hydrochloric acid (14.5 ml). The ether layer was separated and the aqueous layer was further extracted with diethyl ether (2×12 ml). The combined ether phases were washed with water (12 ml), dried ($MgSO_4$) and the solvent removed in vacuo. The resulting products were purified by chromatography (silica gel, neat petroleum ether) to give first as a yellow oil in 37% yield 6-phenyl-1,1,1-trifluoro-3-hexen-5-yne-2-one (**16**) (0.10 g) δ_H 7.55 (2H, dd, J=5.9, 1.8 Hz, *ortho*), 7.41 (3H, m, aromatic), 7.28 (1H, d J=15.8 Hz, H-4). 6.87 (1H, d 15.8, H-3); δ_C 87.30 (C-6), 104.97 (C-5), 116.32 (q, C-1), 121.58 (ArC-1), 127.87 (C-3), 128.84 (ArC-3, ArC-5), 130.52 ArC-4), 131.09 (C-4), 132.60 (ArC-2, ArC-6), 179.42 (q, C-2); δ_F −84.05; ν_{max} 2194, 1722 and 1602 cm^{-1}; found M^+ 224.0444. $C_{12}H_7F_3O$ requires M^+ 224.0449 *m/z* 224 (66), 155 (100), 127 (39), 101 (6) and 77 (16); and then as a yellow oil in 18% yield 1,7-diphenyl-3-hydroxy-3-trifluoromethyl-4-hepten-1,6-diyne (**15**) (0.07 g) δ_H 7.45 (10H, m, aromatic), 6.59 (1H, d J=15.4 Hz, H-4). 6.34 (1H, d 15.4, H-4), 2.98 (1H, brs, OH); δ_C 72.06 (q, C-3), 81.92 (C-6), 86.01(C-1), 89.14 (C-2), 93.79 (C-7), 116.46 (C-5), 120.81 (ArC-1), 122.76 (ArC-1), 123.27 (q, CF_3), 128.58, 128.65, 128.96, 129.85, 131,87, 132.25, (ArC) 134.61 (C-4); δ_F −81.28; ν_{max} 3442, 3059, 2236 and 2205 cm^{-1}; found M^+ 326.0906. $C_{20}H_{13}F_3O$ requires M^+ 326.0918 *m/z* 326 (29), 309 (6), 257 (100), 249 (2), 127 (10), 101 (6) and 77 (9).

1,1,1-Trifluoro-3-tetradecen-5-yn-2-one (20) and 11-(trifluoromethyl)-12-tricosen-9,14-diyn-11-ol (19). To a stirred solution of 1-decyne (0.33 g) in dry ether (4 ml) was added dropwise at room temperature under nitrogen 3 M ethylmagnesium bromide in dry ether (1.60 ml). The mixture was heated under reflux for 1 h and allowed to cool to room temperature. To the stirred solution was added dropwise at room temperature a solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.20 g) in dry ether (3 ml). After heating under reflux for 2 h the reaction was worked up and flash chromatography afforded as a yellow oil in 61% yield 1,1,1-trifluoro-3-tetradecen-5-yn-2-one (**20**) (0.19 g) δ_H 7.05 (1H, dt, J=15.8, 2.2 Hz, H-4), 6.70 (1H, d J=15.8 Hz, H-3). 2.45 (2H, dt 2.2, 7.0, H-7), 1.59 (2H, quin, J=7.1 Hz, H-8) 1.40 (2H, m, H-9), 1.29 (8H, br s H-10, H-11, H-12, H-13), 0.89 (3H, t, J=6.6 Hz, H-14); δ_C179.56 (q, J_{CF}=36 Hz, C-2), 132.41 (C-4), 127.68 (C-3), 116.27 (q, J_{CF}=290 Hz, C-1), 108.51 (C-6), 79.07 (C-5), 31.93, 29.26, 29.15, 29.03, 28.21 and 22.77 (C-8, C-9, C-10, C-11, C-12, C-13), 20.27 (C-7) and 14.18 (C-14); δ_F −83.89; ν_{max} 2929, 2858, 2210, 1723, 1704 and 1597 cm^{-1}; found M^+ 260.1388. $C_{14}H_{19}F_3O$ requires M^+ 260.1388 *m/z* 260 (8), 231 (11), 217 (28), 203 (66), 191 (32), 189 (37), 175 (51), 163 (9), 57 (26), 43 (40) and 29 (16) and as a yellow oil in 17% yield 11-(trifluoromethyl)-12-tricosen-9,14-diyn-11-ol (**19**) (0.08 g) δ_H 6.23 (1H, dt, J=15.8, 2.0 Hz, H-13), 6.04 (1H, d J=15.8 Hz, H-12). 2.78 (1H, br s, OH), 2.33 (2H, dt 1.8, 7.0, H-16), 2.27 (2H, t, J=7.0 Hz, H-8), 1.54 (2H, quin, J=7.0 Hz, H-7, H-17) 1.39 (4H, m, H-6, H-18) 1.29 (16H, br s H-2, H-3, H-4, H-5, H-19, H-20, H-21, H-22), 0.89 (6H, t, J=6.4 Hz, H-1, H-23); δ_C133.78 (C-12), 123.17 (q, J_{CF}=285 Hz, CF_3), 116.58 (C-13), 94.99 (CC), 90.47 (CC), 77.21 (CC), 73.67 (CC), 71.42 (q, J_{CF}=33 Hz, C-11), 31.82, 31.76, 29.16, 29.10, 29.07, 28.94, 28.89, 28.72, 28.50, 28.02 and 22.63 (C-2, C-3, C-4, C-5, C-6, C-7, C-17, C-18, C-19, C-20, C-21 and C-22), 19.44 and 18.55 (C-8 and C-16) and 14.06 (C-1, C-23); δ_F −80.73; ν_{max} 3450, 2928, 2857, 2243 and 2212 cm^{-1}; found M^+ 398.2785. $C_{24}H_{37}F_3O$ requires M^+ 398.2797 *m/z* 398 (1), 341 (1), 329 (100), 299 (4), 273 (4) and 163 (6).

6-Phenyl-1,1,1-trifluoro-3-hexen-5-yne-2-one (16). To a stirred solution of phenylacetylene (0.24 g) in dry ether was added dropwise at −78°C under nitrogen 1.6 M butyllithium in hexanes (1.5 ml). After stirring for 10 min, the mixture was allowed to warm to room temperature and a solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.20 g) in dry ether (4 ml) added. The resulting mixture was heated under reflux for 2 h, worked up and the resulting oil was purified by flash chromatography to afford as a yellow oil 6-phenyl-1,1,1-trifluoro-3-hexen-5-yne-2-one (**16**) (0.10 g) in 37% yield.

4-Phenyl-1,1,1-trifluoro-3-buten-2-one (10) and 4,4-diphenyl-1.1.1-trifluorobutan-2-one (17). A solution of phenylmagnesium bromide was prepared in anhydrous ether from bromobenzene (1.88 g) and dry magnesium turnings (0.29 g). A solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.40 g) in anhydrous ether (12 ml) was added with stirring to the solution of the Grignard reagent at room temperature. The resulting mixture was heated under reflux for 2 h and the cold solution was poured on to 2 M hydrochloric acid (29 ml). The ether layer was separated and the aqueous layer further extracted with diethyl ether (2×24 ml). The combined ether phases were washed with water (24 ml), dried over Na_2SO_4 and the solvent removed in vacuo. The resulting products were purified by chromatography (silica gel, petroleum ether) to give first as a yellow oil in 31% 4-phenyl-1,1,1-trifluoro-3-buten-2-one (**10**) (0.15 g) (see above for physical data); and then as a colourless oil in 15% yield 4,4-diphenyl-1.1.1-trifluorobutan-2-one (**17**) (0.10 g) δ_H 7.09 (10H, m, aromatic), 4.51 (1H, t, J=7.4 Hz, H-4), 3.33 (2H, d J=7.4 Hz, H-3); δ_C 42.65 (C-3), 44.78 (C-4), 115.64 (q, C-1), 127.11, 127.70, 128.99, 142.65 (ArC), 189.49 (q, C-2); δ_F −82.44; ν_{max} 3030, 2903 and1765 cm^{-1}; found M^+278.0920. $C_{16}H_{13}F_3O$ requires M^+ 278.0918 *m/z* 278 (56), 209 (26) and 167 (100).

4,4-Diphenyl-1,1,1-trifluorobutan-2-one (17). A solution of phenylmagnesium bromide was prepared from bromobenzene (0.11 g) and dry magnesium (0.02 g) in ether (0.5 ml). A solution of 4-phenyl-1,1,1-trifluoro-3-buten-2-one (**10**) (0.12 g) in anhydrous ether (3 ml) was added with stirring at room temperature to the Grignard solution under nitrogen. The resulting mixture was heated under reflux for 2 h, and when cold poured into ice cold 2 M hydrochloric acid (7 ml). the ether layer was separated, the aqueous layer further extracted with ether (2×6 ml), the combined ether phases were washed with water (6 ml), dried over $MgSO_4$ and the solvent removed in vacuo.

Chromatography afforded 4,4-diphenyl-1,1,1-trifluorobutan-2-one (**17**) in 65% yield (see above for physical data).

2-Hydroxy-2-methyl-4-phenyl-1,1,1-trifluorobut-3-ene (18). A solution of methylmagnesium iodide was prepared from methyl iodide (0.28 g) and dry magnesium turnings (0.05 g) in anhydrous ether (1.0 ml). A solution of 4-phenyl-1,1,1-trifluoro-3-buten-2-one (**10**) (0.18 g) in anhydrous ether (6 ml) was added with stirring to the solution of the Grignard reagent at room temperature. The resulting mixture was heated under reflux for 2 h and when cold was poured in to ice-cold hydrochloric acid (14.5 ml). The ether layer was separated and the aqueous layer further extracted with ether (2×12 ml). The combined organic phases were washed with water (12 ml), dried over $MgSO_4$ and the solvent removed in vacuo. Chromatography afforded in 72% yield as a yellow oil 2-hydroxy-2-methyl-4-phenyl-1,1,1-trifluorobut-3-ene (**18**) (0.14 g) δ_H 7.38 (5H, m, aromatic), 6.90 (1H, d J=15.8 Hz, H-4), 6.34 (1H, d J=15.8 Hz, H-3) 2.48 (1H, brs, OH), 1.60 (3H, s, CH_3); δ_C 22.35 (CH_3), 74.18 (q, C-2), 125.72 (q, C-1), 126.44 (C-3), 126.99, 128.61, 128.88 (aromatic), 132.34 (C-4), 135.78 (aromatic); δ_F −79.66; ν_{max} 3422, 3030, 2998, 2946 cm^{-1}; found M^+ 216.0751. $C_{11}H_{11}F_3O$ requires M^+ 216.0762 *m*/*z* 216 (14), 201 (5) and 147 (40).

4-Phenyl-1,1,1,-trifluoro-3-buten-2-one (10). Phenyllithium (1.8 M) in cyclohexane: ether (70:30, 1.33 ml) was added dropwise with stirring to a solution of 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**4**) (0.20 g) in ether (6 ml) at room temperature under nitrogen. The resulting mixture was heated under reflux for 2 h, and when cold was poured in to ice-cold hydrochloric acid (14.5 ml). The ether layer was separated and the aqueous layer further extracted with ether (2×12 ml). The combined ether phases were washed with water (12 ml), dried over $MgSO_4$ and the solvent removed in vacuo. Chromatography afforded in 42% yield as a yellow oil 4-phenyl-1,1,1,-trifluoro-3-buten-2-one (**10**) (0.10 g) (see above for spectroscopic data).

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