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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

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Published online: 24 Sep 2006.

To cite this article: Jean-Pierre Bégué , Danièle Bonnet-Delpon & Anukwadey Dogbeavou (1992) Efficient Procedure to 4-Carbethoxy-3-Trifluoro Methylcyclohex-2-Enone and 4-Alkylated Derivatives, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 22:4, 573-579, DOI: 10.1080/00397919208019256

To link to this article: http://dx.doi.org/10.1080/00397919208019256

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EFFICIENT PROCEDURE TO 4-CARBETHOXY-3-TRIFLUORO METHYLCYCLOHEX-2-ENONE AND 4-ALKYLATED DERIVATIVES

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The 4-carbethoxy-3-trifluoromethylcyclohex-2-enone <u>1a</u> was prepared in one-pot procedure in 90 % yield, from ethyl trifluoroacetoacetate (ETFAAE) and methylvinyl ketone. This reaction has been extended to alkylated ethyl trifluoroacetoacetate.

A recent communication describes a two-step preparation of 4-carbethoxy-3-trifluoromethylcyclohex-2-enone <u>1a</u> in limited yield [1]. This prompts us to report our own results on a simple one-pot preparation of this compound.

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In the scope of studies on ethyl trifluoroacetoacetate (ETFAAE) as starting material to trifluoromethylated synthons [2,3,4], we are developing its conjugated addition to Michael acceptors. In this way, we have performed this reaction with methylvinylketone. In EtO-/EtOH conditions, this reaction has been described either to undergo a di-addition of the methylvinylketone [5],or to give a trifluoromethylated β -ketol in moderate yield [1]. We describe here that the use of HNa in catalytic amount allows the stop of the reaction at the 1,5-diketone <u>2a</u> step [6]. <u>2a</u> can be isolated in a high yield (90 %) after 4 hours of reaction at room temperature. This diketone could be directly transformed to trifluoromethylated cyclohexenone <u>1a</u> in very good yield (90%), by reflux in presence of piperidinium acetate. So, this classical catalyst of aldolisation-crotonisation reaction [6,7], is very efficient to perform the dehydration of the trifluoromethylated β -ketol whereas acidic conditions give only limited yield [1].



A one pot procedure has been devised from this results. After formation of <u>2a</u>, addition of a small amount of piperidine acetate to the reaction followed by 20 hours reflux gives directly, the cyclohexenone <u>1a</u> in 92 % yield.

This same procedure has been performed on various α -substituted ethyl trifluoroacetoacetates, leading to 4-alkyl-4-carbethoxy-3-trifluoromethyl-cyclohex-2-enones <u>1b,c,d</u>.

This one pot procedure highly improves the preparation of trifluoromethylated cyclohexenones $\underline{1}$ in regard to both its easiness and its yield.

One pot synthesis of 4-Carbethoxy-3-trifluoromethylcyclohex-2-enone 1a.

Ethyl trifluoroacetoacetate (20 g; 0.108 mol) and methylvinylketone (8.4 g; 0.12 mol) were added to a stirred suspension of sodium hydride (2.75 mmol) in benzene (90 mL). After 4 hours, 0.5 mL of acetic acid and 0.5 mL of piperidine were added and the mixture was refluxed for 24 hours. The solvent was removed under vacuum and the crude product was distilled under reduced pressure yielding 23 g (92%) of <u>1a</u>.

bp_{20mmHg}: 120°C.

NMR 19 F (188.3 MHz) δ : -69.2 (s).

¹H (200 MHz) δ: 1.29 (t, J = 7.2 Hz, 3 H, OEt); 2.5 (m, 4 H, 2xCH₂); 3.6 (t, J = 2.6 Hz, 1 H, CH-COOEt); 4.23 (q, 7 Hz, 2 H, OEt); 6.49 (s, 1 H). ¹³C (50 MHz) δ : 13.9 ; 26.3; 33.7; 38.9; 62.0; 122.4 (q, J_{CF} = 274.4 Hz, CF₃); 130.3 (q, ⁴J_{CF} = 4.76 Hz, *C*=C-CF₃); 143.4 (q, ³J_{CF} = 32 Hz, C=C-CF₃); 169.6; 196.7.

MS (70 eV) m/e: 237 (M+1, 100%); 208 (35%); 163 (40%) 95 (44%).

3-Carbethoxy-1,1,1-trifluoroheptan-2,6-dione 2a.

¹⁹F δ: -77.6

NMR

Ethyl trifluoroacetoacetate (4g ; 0.0216 mol) and methylvinylketone (1.7g ; 0.024 mol) were added to a stirred supension of sodium hydride (0.55 mmol) in benzene (20 mL). After 4 hours of stirring, the mixture was filtered on SiO₂, concentrated under vacuum and distilled bulb to bulb (110°C) to give 4.9 g (90%) of the diketone <u>2a</u>.

Anal. calcd for C₁₀H₁₃F₃O₄: C, 47.24; H, 5.12. Found: C, 46.81; H, 5.01.

Synthesis of 4-Carbethoxy-3-trifluoromethylcyclohex-2-enone 1a from 2a.

The 1,5-diketone 2a (2 g, 7.9 mmol) and five drops of acetic acid and 5 drops of piperidine in 15 mL of benzene were refluxed for 12 hours. After evaporation of benzene, 30 mL of ether was added. After washing with brine

 $(2 \times 15 \text{ mL})$ and drying on magnesium sulfate, the organic phase was concentrated under vacuum. 1.9 g of the crude product was purified by chromatography on silicagel, (Pentane-Ether 4:1), yielding 1.6 g (90 %) of <u>1a</u>.

4-Carboethoxy-4-methyl-3-trifluoromethylcyclohex-2-enone 1b

Silicagel chromatography : (Pentane-ether 5:1); Yield : 90%.

NMR ¹⁹F δ: -63.3.

¹H δ: 1.2 (t, J = 7.1 Hz, 3 H, OEt); 1.5 (s, 3 H, CH₃); 2.4 (m, 4xCH₂); 4.2 (m, 2 H, OEt); 6.4 (s, HC=C-CF₃).

¹³C δ : 13.7; 21.8; 33.9; 35.3; 43.8; 61.8; 122.5 (q, J_{CF} = 276.5 Hz, CF₃); 130.3 (q, ⁴J_{CF} = 5.2 Hz, C=C-CF₃); 147.8 (q, ³J_{CF} = 29.5 Hz, C=C-CF₃); 172.0; 196.8.

MS (70 eV) m/e: 251 (M+1, 51%); 178 (45%); 109 (100%).

Anal. calcd for C₁₁H₁₃F₃O₃: C, 52.80; H, 5.20. Found: C, 52.42; H, 4.99.

4-Benzyl-4-carbethoxy-3-trifluoromethylcyclohex-2-enone 1c.

Silicagel chromatography : (Pentane-Ether 1:2); Yield : 88 % RMN 19 F δ : -60.0.

¹H δ : 1.4 (t, 3 H, J = 7 Hz, OEt); 1.9 (m, 2H, CH₂); 2.4(m, 2H, CH₂); 3.2 (d, J_{AB} = 14.2 Hz, 1 H, H_A-CH-C₆H₅); 3.7 (d, J_{AB} = 14.2 Hz, 1 H, H_B-CH-C₆H₅); 4.3 (m, 2 H, OEt); 6.6 (s, 1 H, CH=C-CF₃); 7.3 (5 H arom.).

¹³C δ : 13.9; 31.3; 33.4; 40.5; 48.5; 62.3; 123.0 (q, $J_{CF} = 277$ Hz, CF₃); 127.4; 128.5; 130.4; 132.9 (q, ${}^{4}J_{CF} = 4.8$ Hz, *C*=C-CF₃); 135.3; 147.7 (q, ${}^{3}J_{CF} = 29.3$ Hz, CH=*C*-CF₃); 172.3; 196.9. MS $m/e 326 (M^+, 1\%); 235 (2\%); 91 (100\%).$

Anal.calcd for C17H17F3O3: C, 62.57; H, 5.21. Found: C, 62.36; H, 5.04.

4-Allyl-4-carboethoxy-3-trifluoromethylcyclohex-2-enone 1d.

Silicagel chromatography : (Pentane-Ether 3:1); Yield : 90%.

RMN 19 F δ : -62.6.

¹H δ : 1.2 (t, J = 7 Hz, 3 H); 2.3 (m, 2 H, CH₂); 2.6 (m, 2 H, CH₂-C=C); 2.8 (m, CH₂); 4.3 (m, 2 H, OEt); 5.2 (d, 2 H, CH=CH₂); 5.8 (m, 1 H, HC=CH₂); 6.6 (s, 1 H, CH=C-CF₃). ¹³C δ : 13.8; 31.2; 33.6; 39.3; 47.5; 62.0; 120.3; 123.0 (q, J_{CF} = 276.9 Hz, CF₃); 132 (q, ³J_{CF} = 5.1 Hz, C=C-CF₃); 132.3; 147.2 (q, ³J_{CF} = 29.7 Hz, C=C-CF₃); 171.8; 197.0.

MS $(70 \text{ eV}) \text{ m/e: } 276 (M^+, 19\%); 203 (95\%); 163 (28\%).$

Anal. calcd for C₁₃H₁₅F₃O₃: C, 56.52; H, 5.43. Found: C, 56.45; H, 5.35.

References

- [1] Tordeux, M.; Wakselman, C. Synthetic Comm. 1991, 21, 1243.
- [2] Aubert, C.; Bégué, J.P.; Charpentier-Morize, M.; Née, G.; Langlois, B. J. Fluorine Chem. 1989, 44, 361.
- [3] Aubert, C.; Bégué, J.P.; Charpentier-Morize, M.; Née, G.; Langlois, B. J. Fluorine Chem. 1989, 44, 377.
- [4] Bégué, J.P.; Bonnet-Delpon, D.; Lequeux, T. J. Chem. Soc. Perkin Trans. 1, Accepted for publication.

- [5] Ostaszynsky, A. Bull. Acad. Pol. Sci., ser. Sci. Chim. 1960, 8, 619.
- [6] Kreiser, W.; Below, P. Tetrahedron Lett. 1981, 429.
- [7] Mead, D.; Loh, R.; Asato, A.E.; Liu, R.S.H. Tetrahedron Lett. 1985, 26, 2873.

(Received in UK 23 August, 1991)