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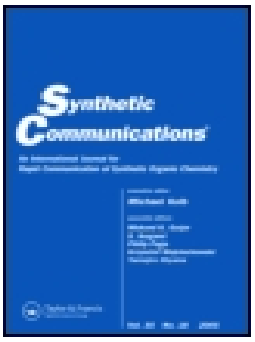

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UMPOLUNG OF TROPONE: PREPARATION OF 2-AROYL- AND 2-ACYLTROPONES

Hiroshi Horikoshi, Hiroyuki Miyano, Tohru Takayasu, Makoto Nitta*
Department of Chemistry, School of Science and Engineering,
Waseda University, Shinjuku-ku, Tokyo 169-8555, Japan

Abstract: The reaction of 2-chlorotropone with DIBAH followed by aldolization with several aldehydes affords 2-(1-hydroxyalkyl)tropones, subsequent oxidation of which results in the formation of 2-aroyl- and 2-acyltropones.

Tropone and its derivatives are easily attacked by nucleophiles.[1-3] Several examples of the C-C bond-forming reactions of 2-halotropones with carbanions,[1] Grignard,[4,5] organo lithium,[4,6] and organo copper[7] reagents, and lithium enolates [8] have been reported to give 2-substituted tropones. Recently, Banwell has also reported effective palladium-mediated ipso-substitution of bromotropolones with aryl-, alkenyl-, and alkyltrimethylstannanes to introduce a carbon substituent into the tropone nucleus.[9] Although the resistant nature of the tropone nucleus toward electrophilic attack is generally recognized,[1,2,10] we have previously reported a reverse polarity (umpolung) strategy for realizing a formal electrophilic substitution of tropone. The reaction of 2-chlorotropone (**1**) with $LiAlH_4$ or $LiAlH(O^tBu)_3$ gives 2-chlorocycloheptadienone enolate (**2**), the structure of which is elucidated by

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*To whom correspondence should be addressed

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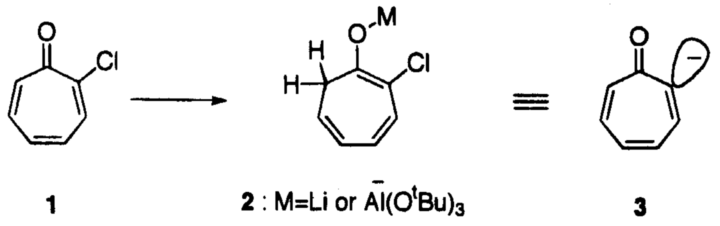
Scheme 1

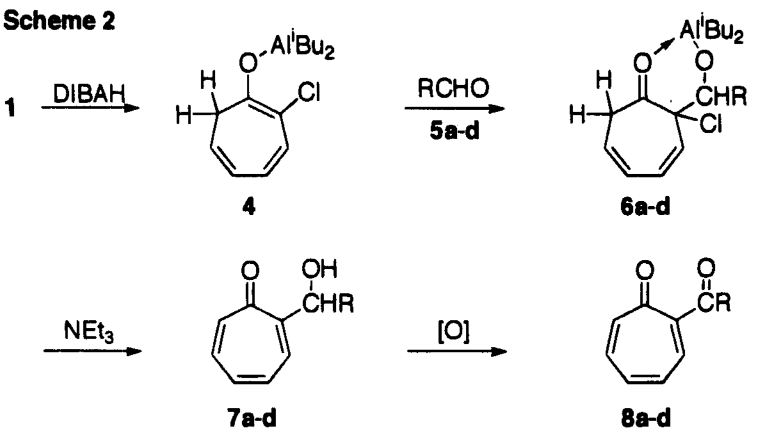


1 2 : M=Li or $\bar{A}l(O^tBu)_3$ 3

the ^1H NMR spectra, and it reacts with tropylium and several organic cations to give 2-substituted tropones in good yields.[11] Thus, the enolate (**2**) is considered to be an equivalent of the 2-troponide ion (**3**) (Scheme 1). Although (tricarbonyltropone)iron has been reported to undergo the Friedel-Crafts acetylation,[12] tropone and tropolone are known not to undergo the Friedel-Crafts substitution reaction.[13] In this paper, we describe a convenient preparation of 2-aroyl- and 2-acyltropones by using aldolization of diisobutylaluminum 2-chloro-1,3,5-cycloheptatrienolate (**4**), which is prepared *in situ* by the reaction of 2-chlorotropone (**1**) with DIBAH, with several aldehydes and subsequent oxidation.

The reaction of 2-chlorotropone (**1**) with DIBAH was carried out in tetrahydrofuran (THF), and the mixture was subsequently reacted with excess amount of aldehydes (**5a-d**) and then NEt_3 at room temperature to give

Scheme 2



a : $R=4\text{-}CNC_6H_4$; **b** : $R=C_6H_5$; **c** : $R=4\text{-}MeOC_6H_4$; **d** : $R=Et$

2-(hydroxyalkyl)tropones (**7a-d**) in modest yields (Scheme 2). The results are summarized in Table 1. The reaction is considered to proceed via the enol ether (**4**) and subsequently the intermediate (**6**). 4-Cyanobenzaldehyde (**5a**) gives a slightly better yield of **7a** (Run 1 in Table 1) as compared with **5b,c** (Run 2 and 3 in Table 1). Even the reaction of **4** with enolizable aldehyde (**5d**) gave the adduct **7d** (Run 4 in Table 1).

Table 1. Aldolization of 2-chlorotropone (**1**) with aldehydes (**5a-d**) and subsequent oxidation.

		Aldolization		Oxidation	
Run	Aldehyde	Product	Yield/%	Product	Yield/%
1	**5a**	**7a**	35	**8a**	83
2	**5b**	**7b**	31	**8b**	67(81)[a)]
3	**5c**	**7c**	31	**8c**	77
4	**5d**	**7d**	36	**8d**	70

a) Yield obtained by using chromium trioxide.

The compound **7a** is known and the structural assignment was based on the comparison of the physical data with those reported in the literature.[14] The structures of **7b-d** were also deduced from the spectral data as well as from the comparison of their spectral data with those of **7a**..

On the Swern oxidation[15] or chromium trioxide oxidation, compounds (**7a-d**) were converted to 2-benzoyltropone derivatives (**8a-c**) and 2-propanoyltropone (**8d**) in moderate yields, which are also summarized in Table 1. The compounds (**8a**)[14] and (**8c**)[16] are known compounds and their physical data are in agreement with those reported in the literature. Comparison of the spectral data of new compounds (**8b,d**) with those of (**8a,c**) easily revealed the structures of (**8b,d**).One may consider that the reaction of **1** with DIBAH, followed by addition of acid chlorides and NEt_3 directly gives 2-aroyl- and 2-acyltropones. However, attempted reaction of **4** with benzoyl chloride did not give **8a**, and tropone, which derives from the reaction of **4** with NEt_3, was obtained in 80-85% yield.

The 2-benzoyltropone derivatives, which have a strong electron-withdrawing group, such as 4-cyanophenyl-, 4-nitrophenyl-, and 2-nitrophenyl groups, have been prepared through the base-prompted reaction of the corresponding benzyoxytropones.[14] Although the palladium-catalyzed carbonylative coupling of the troponyltriflate with alkenyl- and arylstannanes in the presence of carbon monoxide has afforded tropon-2-yl ketones in modest yields,[16] the present reaction using 2-chlorotropone (**1**), DIBAH, and aldehydes provides a convenient methodology for the preparation of hitherto not easily accessible 2-aroyl- and 2-acyltropones, albeit in modest total yields.

Experimental

The IR spectra were recorded on a Shimadzu IR-400 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a Hitachi R-90 spectrometer, and the chemical shifts are given in ppm (δ) relative to $SiMe_4$ standard: *J*-values are given in Hz. Mass and high-resolution mass spectral studies were run on Shimadzu GCMS-QP1000 and JEOL DX300 spectrometers. Melting points are uncorrected.

General Preparation of 10a-d. To a stirred solution of **1** (281 mg, 2 mmol) in THF (3 mL) was added DIBAH (2.4 mmol, 2.4 mL of 1.0 mol/l hexane solution) at 0℃, and the mixture was warmed up to room temperature, and stirred for another 30 min under a nitrogen atmosphere. After addition of aldehydes **5a-d** (4.0 mmol) to the reaction mixture, and it was stirred for 1 h; then triethylamine (342 mg, 2.4 mmol) and methanol (20 mL) were added to the mixture. The reaction mixture was then filtered through Celite and the filtrate was concentrated. The resulting residue was separated by TLC on silica gel (hexane:AcOEt = 1:1) to give the products **7a-d**. The results are summarized in Table 1.

2-[(4-Cyanophenyl)hydroxymethyl]tropone (**7a**): mp 130-131 ℃ (from ethanol) [lit.[14] mp 132-133 ℃ (from AcOEt)].

2-(Phenylhydroxymethyl)tropone (**7b**): oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ: 4.20-5.15 (1H, broad s), 6.70-7.04 (4H, m), 7.04-7.60 (6H, m); IR ($CHCl_3$) ν 1625, 1565 cm^{-1}; MS(*m/z*) 212 (M^+, 54), 105 (100); HRMS: calcd for $C_{14}H_{12}O_2$, 212.0838, found 212.0858

2-[(4-Methoxyphenyl)hydroxymethyl]tropone (**7c**); mp 115-116 °C (from ethanol); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 3.77 (3H, s), 4.23 (1H, d, *J*=5.5), 5.82 (1H, d, *J*=5.5), 6.95-7.55 (9H, m); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ: 55.1, 74.8, 113.7 (2C), 127.8 (2C), 133.7, 133.8, 133.9, 134.3, 135.7, 141.5, 154.6, 159.0, 187.1; IR ($CHCl_3$) ν: 1630, 1610, 1560 cm^{-1}; MS(*m/z*) 242 M^+, 52), 135 (100); HRMS: cacld for $C_{15}H_{14}O_3$ 242.0943, found 242.0988.

2-(1-Hydroxypropyl)tropone (**7d**): oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ: 0.98 (3H, t, *J*=7.4), 1.58-2.10 (2H, m), 3.82-4.11 (1H, m), 4.55-4.73 (1H, m), 6.96-7.25 (4H, m), 7.27-7.52 (1H, m); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ: 10.5, 29.3, 75.4, 133.5, 133.9, 134.1, 135.7, 141.2, 155.2, 187.2; IR ($CHCl_3$) ν 1625, 1545 cm^{-1}; MS(*m/z*) 164 (M^+, 34), 135 (100); HRMS :calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0834.

General Preparation of 8a-d. (A): Swern oxidation was performed as described in the literature.[15] (B) Oxidation of **7b** with CrO_3: To a stirred solution of CrO_3 in 1 mol/L H_2SO_4 (3 mL) and acetone (2 mL) was added **7b** (85 mg, 0.4 mmol) in acetone (1 mL), and the mixture was stirred at room temperature for 1 h. To th reaction mixture was added H_2O, extracted with benzene, and the extract was dried over Na_2SO_4, and concentrated. The residue was then purified by TLC on silica gel (hexane:AcOEt = 1:1) to give **8b** (68 mg, 81%). The results are summarized in Table 1.

2-(4-Cyanobenzoyl)tropone (**8a**): mp 164-166 °C (from ethanol) (lit.[14] mp 166-168 °C).

2-Benzoyltropone (**8b**): yellow crystals; mp 60-63 °C (from hexane-ether); ^{1}H NMR (90 MHz, $CDCl_3$) δ 6.87-7.60 (8H, m), 7.60-7.96 (2H, m); ^{13}C NMR ($CDCl_3$) δ 128.2 (2C), 128.9 (2C), 133.1, 133.6, 134.6, 135.3, 135.8, 136.1, 142.7, 150.9, 185.4, 195.5; IR ($CHCl_3$) ν 1668, 1626, 1582, cm^{-1}; MS(*m/z*) 210 (M^+, 7), 77 (100); HRMS: calcd for $C_{14}H_{10}O_2$ 210.0680, found 210.0662.

2-(4-Methoxybenzoyl)tropone (**8c**): light yellow crystals; mp 130-132 °C (from ethanol) (lit.[16] mp 132-133 °C).

2-Propanoyltropone (**8d**); oil; ^1H NMR (90 MHz, $CDCl_3$) δ 1.15 (3H, t, *J*=7.3), 2.83 (2H, q, *J*=7.3), 7.05-7.23 (4H, m), 7.34-7.59 (1H, m); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ 8.4, 34.5, 133.4, 135.1, 135.2, 136.2, 143.1, 150.2, 185.6, 204.8; IR (film) ν 1694, 1630, 1570 cm^{-1}; MS(*m/z*) 162 (M^+, 54), 105 (100); HRMS calcd for $C_{10}H_{10}O_2$ 162.0681, found 162.0686

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