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# Reaction of $\beta$ -halo $\alpha$ , $\beta$ -unsaturated ketones with cuprate reagents. Efficient syntheses of $\beta$ , $\beta$ -dialkyl ketones and $\beta$ -alkyl $\alpha$ , $\beta$ -unsaturated ketones. A synthesis of (Z)-jasmone

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Received November 13, 1981

EDWARD PIERS, KIN FAI CHENG, and ISAO NAGAKURA. Can. J. Chem. 60, 1256 (1982).

Treatment of the 3-halo-2-cyclohexen-1-ones 11–15 and 17 with an excess of lithium dimethylcuprate provided good to excellent yields of the corresponding 3,3-dimethylcyclohexanones 21–24. Similar reactions involving the  $\beta$ -bromo cyclohexenones 19 and 20 stopped at the monoaddition stage, producing the cyclopentenones 40 and 43. Reaction of the  $\beta$ -bromo cyclohexenones 12 and 15 with 1.1 equiv. of lithium dimethylcuprate did not effect clean conversion of these substrates into the corresponding 3-methyl-2-cyclohexen-1-ones. When a series of  $\beta$ -bromo enones 12, 14–19 were allowed to react with the lithium (phenylthio)(al-kyl)cuprates 44–47, the corresponding  $\beta$ -alkyl enones were, in general, produced cleanly and efficiently. However, reaction of 3-bromo-2-methyl-2-cyclopenten-1-one (19) with the cuprate reagent 44 gave mainly the  $\beta$ -phenylthio enone 49. This undesired result could be avoided by employing, in the place of 19, the  $\beta$ -bromo-2-cyclohexen-1-one (14) with 3 equiv. of the mixed high yield of 2,3-dimethyl-2-cyclopenten-1-one (32). Alkylation of 1,3-cyclopentanedione with (Z)-1-chloro-2-penten afforded compound 51, which was converted into the  $\beta$ -bromo enone 52. Treatment of the latter substance with lithium dimethylcuprate provided (Z)-jasmone (53).

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Les halo-3 cyclohexène-2 ones-1 (11–15 et 17) réagissent avec le diméthylcuprate de lithium en excès en donnant les diméthyl-3,3 cyclohexanones correspondantes avec des rendements variables. Des réactions analogues mettant en jeu les  $\beta$ -bromo cyclopentènones (19 et 20) s'arrêtent à l'étape de monoaddition en produisant les cyclopentènones (40 et 43). La réaction des  $\beta$ -bromo cyclohexènones (12 et 15) avec 1,1 équivalent de diméthylcuprate de lithium n'affectent pas la transformation franche de ces substrats en méthyl-3 cyclohexène-2 ones-1 correspondantes. Quand on fait réagir une série de  $\beta$ -bromo ènones (12, 14–19) avec les (phenylthioalkyl)cuprates de lithium (44–47), on obtient en général les  $\beta$ -alkylènones correspondantes d'une manière efficace et pure. Cependant, la bromo-3 méthyl-2 cyclopentène-2 one-1 (19) réagit avec le cuprate 44 en donnant principalement la  $\beta$ -phénylthioénone 49. On peut éviter ce produit indésirable en remplaçant le produit 19 par la  $\beta$ -iodo cyclopentène-0 one-1 (40). La bromo-3 cyclohexène-2 one-1 (14) réagit avec 3 équivalents du vinylcuprate mixte (48) en donnant la (butène-3 yl)-3 cyclohexène-2 one-1 (32). L'alkylation de la cyclopentanedione-1,3 avec le (Z) chloro-1 pentène-2 conduit au composé 51 que l'on transforme en  $\beta$ -bromo ènone (52). Cette dernière réagit avec le diméthylcuprate de lithium en donnant la (Z)-jasmone (53).

[Traduit par le journal]

## Introduction

The reaction outlined in general terms by eq. [1] has been employed a great deal in organic synthesis, particularly in the very recent past. In this process, a  $\beta$ -substituted  $\alpha$ , $\beta$ -unsaturated ketone 1 reacts with a nucleophilic species (or an electrontransfer reagent) to provide initially the conjugate addition intermediate 2. If Y is a good leaving group, it will be expelled from this intermediate to provide the product 3. Thus, in an overall sense, a substitution reaction has occurred and, as such, the  $\beta$ -substituted enone 1 acts as a synthetic equivalent to the unsaturated  $a^3$  synthon 5 (normal reactivity) (1). On the other hand, if the initially formed product 3 were to react in a conjugate addition sense with a second equivalent of reagent, the final product would be the ketone 4. In this case, the





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try	Starting material	Equivalents of Me <sub>2</sub> CuLi	Reaction conditions	Product(s) (ratio) <sup>a</sup>	Yield (%) <sup>b</sup>
1	11	3	0°C, 1 h	21	82
2	12	3	0°C, 1 h	21	86
3	13	3	0°C, 1 h	21	84
4	14	3	0°C, 1 h	22	74
5	15	3	0°C, 1 h	23	61
5	17	6	0°C, 10 min; room temp., 15 min	<b>24</b> + <b>38</b> (9:1)	65
7	19	3	0°C, 1 h	40	56
3	20	2	0°C, 30 min	43	68
)	12	1.1	0°C, 10 min	<b>21 + 25</b> (10:86) <sup>c</sup>	86
)	12	1.1	-78°C, 10 min	<b>21</b> + <b>25</b> (3:97)	87
1	15	1.1	0°C, 15 min	33	51 <sup>d</sup>

TABLE 1.	Reaction of	β-halo α.	<b>B</b> -unsaturated	ketones wi	ith lithium	dimethyle	cuprate
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<sup>a</sup> Where pertinent, the ratio of products was determined by glc. <sup>b</sup>Yield of distilled product(s). <sup>c</sup>This product mixture also contained ~4% of the starting material 12. <sup>d</sup>Starting material 15 (31%) was recovered.

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original  $\beta$ -substituted enone 1 would be serving as the equivalent to the  $a^3-a^3$  synthon 6.

With respect to the nature of Y in eq. [1], a variety of functional groups have been employed successfully: chloro (2-19), bromo (14, 16, 20), alkylthio (21-27), alkylsulfinyl (27, 28), acyloxy (29), alkoxy (23, 30), tosyloxy (31, 32), mesyloxy (33), and diethylphosphonoxy (34). It is clear from a perusal of the chemical literature that the synthetic utility of  $\beta$ -chloro enones has been particularly well established, since the chloro substituent has been displaced successfully by a wide variety of oxygen, nitrogen, sulfur, and carbon nucleophiles (2-19). Until recently, however, efficient substitution of the chloro group by *carbon* nucleophiles had been accomplished only when the carbanions were relatively highly stabilized (e.g. conjugate bases of malonic ester derivatives,  $\beta$ -keto esters, trimethylsulfoxonium chloride, etc.). Obviously, the products of these reactions were enones containing highly functionalized substituents at the  $\beta$  carbon. Although the preparation of structurally simpler  $\beta$ -alkyl or  $\beta$ -alkenyl  $\alpha$ ,  $\beta$ -unsaturated ketones had been accomplished by the reaction of  $\beta$ -chloro enones with dialkyl- or dialkenylcadmium reagents, the yields were generally poor to mediocre (2).

Recently, we described a new, general method for the preparation of  $\beta$ -halo  $\alpha$ ,  $\beta$ -unsaturated ketones 8 (35). This method, which involved the reaction of 1,3-diketones 7 with triphenylphosphine dihalides in the presence of triethylamine (eq. [2]), not only provided high yields of  $\beta$ -chloro and  $\beta$ -bromo enones, but also constituted the first general procedure for the preparation of cyclic  $\beta$ -iodo  $\alpha$ ,  $\beta$ -unsaturated ketones, a previously unknown class of compounds. We report herein that cyclic  $\beta$ -halo enones 8, particularly the bromo and iodo derivatives, react smoothly and efficiently with a variety of organocuprate reagents to pro-



duce the corresponding  $\beta$ , $\beta$ -dialkyl 9 or, more importantly, the corresponding  $\beta$ -alkyl  $\alpha$ ,  $\beta$ -unsaturated ketones  $10^{2,3}$  (eq. [3]). As such, the  $\beta$ -halo



enones 8 serve as excellent synthetic equivalents to the unsaturated  $a^3$  synthon 5 and the  $a^3-a^3$  synthon 6.

## **Results and discussion**

## (a) Reaction of cyclic $\beta$ -halo enones with lithium dimethylcuprate

Our initial work in this area involved a brief study of the use of an excess of the reagent lithium dimethylcuprate (Me<sub>2</sub>CuLi) with the expectation that the  $\beta$ -halo enones would be transformed into the corresponding  $\beta$ ,  $\beta$ -dimethyl ketones (cf. 8  $\rightarrow$ 9). The results of some of these experiments are summarized in Table 1. Thus, reaction of 3-chloro-5,5-dimethyl-2-cyclohexen-1-one (11) (see Chart 1)

<sup>&</sup>lt;sup>2</sup>For a preliminary account of some of the work reported herein, see ref. 36.

<sup>&</sup>lt;sup>3</sup>Prior to our initial communication (36), the reaction of  $\beta$ -halo enones with cuprate reagents had not been described. Subsequently, a few examples of the reaction of  $\beta$ -chloro and/or β-bromo enones with lithium dialkylcuprates or related reagents have been reported (5b, 13, 14, 16). It should be noted also that similar transformations have been accomplished with β-alkylthio (21–25),  $\beta$ -acetoxy (29),  $\beta$ -alkoxy (23),  $\beta$ -diethylphosphonoxy (34), and  $\beta$ -mesyloxy (33) enones.

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with 3 equivalents of Me<sub>2</sub>CuLi at 0°C gave an excellent yield of 3,3,5,5-tetramethylcyclohexanone (21) (Table 1, Entry 1). Similarly the corresponding  $\beta$ -bromo and  $\beta$ -iodo enones 12 and 13 were also smoothly converted into the ketone 21, and the substituted cyclohexanones 22 and 23 could be obtained readily from the  $\beta$ -bromo enones 14 and 15, respectively (Entries 2-5). In contrast, attempted conversion, under identical reaction conditions, of 3-bromo-2-(2-cyanoethyl)-2-cyclohexen-1-one (17) into the corresponding  $\beta$ , $\beta$ -dimethyl cyclohexanone derivative 24 gave only a poor yield ( $\sim 25\%$ ) of a mixture of products, which included, in addition to the expected compound 24, a significant amount of the enone 38. However, when a greater excess (6 equiv.) of reagent was employed and the reaction conditions were altered somewhat, a reasonable yield of the desired product 24 (contaminated with a small amount of the enone 38) was realized (Entry 6). Thus, although these experiments do not constitute an extensive investigation, it appears that substituted 3-halo-2-cyclohexen-1-ones can serve as convenient precursors for the preparation of the corresponding 3,3-dialkylcyclohexanone systems.

In contrast to these results involving sixmembered ring substrates, reaction of the  $\beta$ -bromo cyclopentenones **19** and **20** with excess Me<sub>2</sub>CuLi did not result in the formation of the corresponding  $\beta$ , $\beta$ -dimethyl cyclopentanones. Instead, in both cases, the reaction stopped at the monoaddition stage, and the products were identified as the cyclopentenones **40** and **43** (Entries 7, 8). It is thus clear that conjugate addition of Me<sub>2</sub>CuLi to 2,3disubstituted cyclopentenones is not as facile a process as the corresponding reaction involving 2,3-disubstituted cyclohexanones. From a strictly synthetic point of view, it is pertinent to note that the reaction of 2-alkyl-3-bromo-2-cyclopenten-1ones with Me<sub>2</sub>CuLi constitutes an efficient method for preparing 2-alkyl-3-methyl-2-cyclopenten-1ones. This reaction was subsequently applied to a synthesis of (Z)-jasmone (*vide infra*).

In an effort to determine whether or not the reaction of β-bromo cyclohexenones with Me<sub>2</sub>CuLi could be controlled so as to produce only the corresponding 3-methyl-2-cyclohexen-1-ones (cf. 8  $\rightarrow$  10), the reactions of the  $\beta$ -bromo enones 12 and 15 with slightly more than 1 equivalent of the cuprate reagent were investigated. When 12 was allowed to react with 1.1 equivalents of Me<sub>2</sub>CuLi at 0°C for 10 min, the major product was the desired 3,5,5-trimethyl-2-cyclohexen-1-one (25). However, a small amount of starting material was recovered and, in addition, a significant quantity of the "double addition" product 21 was also formed (Entry 9). When the reaction temperature was lowered to -78°C an improvement was noted, but the product still contained a small amount of the tetramethylcyclohexanone 21 (Entry 10). Furthermore, reaction of 3-bromo-2-methyl-2-cyclohexen-1-one (15) with 1.1 equivalents of Me<sub>2</sub>CuLi at 0°C for 15 min gave only a 51% yield of the desired enone 33, along with 31% of the starting material (Entry 11). Longer reaction times led to the disappearance of nearly all of the starting material, but also produced small amounts of the trimethylcyclohexanone 23.

In view of these results, it was decided to investigate the use of a different type of cuprate reagent with the aim of developing a better method for effecting the clean, efficient conversion of cyclic  $\beta$ -bromo enones into the corresponding

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Can. J. Chem, Downloaded from www.mrcresearchpress.com by 80.82.77.83 on 03/04/18 For personal use only.  $\beta$ -alkyl enones. After some investigation, we found that lithium (phenylthio)(alkyl)cuprate reagents (37, 38) are generally excellent for this purpose, and the next section of this paper describes the results of this study.

## (b) Reaction of cyclic $\beta$ -bromo enones with lithium (phenylthio)(alkyl)cuprates

Solutions of the mixed cuprate reagents 44–48 employed in this study were prepared simply by addition of a solution of the appropriate alkyllithium (or vinyllithium) to a stirred suspension of (phenylthio)copper in dry tetrahydrofuran at  $-20^{\circ}$ C (37, 38). The reactions of these reagents with a number of cyclic β-bromo enones were investigated (see Chart 1 and Table 2).

[C <sub>6</sub> H <sub>5</sub> SCuR]Li				
44	R = Me			
45	$\mathbf{R} = n \cdot \mathbf{B} \mathbf{u}$			
46	$\mathbf{R} = sec$ -Bu			
47	$\mathbf{R} = t - \mathbf{B}\mathbf{u}$			
48	$R = CH = CH_2$			

In connection with the experiments summarized in Table 2, a number of points should be noted. In some of the experiments involving the cuprate reagents 44-47 (Entries 1-17), the distilled products contained small amounts of starting material (generally < 5%). However, in no case were we able to detect any product resulting from further

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TABLE 2. Reaction of  $\beta$ -bromo  $\alpha$ ,  $\beta$ -unsaturated ketones with lithium (phenylthio)(alkyl)cuprates

Entry	β-Bromo enone	Cuprate reagent <sup>a</sup>	Reaction temperature (°C) <sup>b</sup>	Product (% yield) <sup>c</sup>
1	12	44	0	25 (94)
2	14	44	0	28 (82)
3	15	44	0	33 (70)
4	16	44	0	37 (83)
5	17	44	0	<b>38</b> (76)
6	19	44	0	<b>40</b> (15) <sup>d</sup>
7	12	45	-20	<b>26</b> (93)
8	14	45	-20	<b>29</b> (84)
9	15	45	-20	34 (87)
10	19	45	-20	<b>41</b> (64)
11	14	46	-78	30 (91)
12	15	46	-20	35 (82)
13	12	47	0	27 (89)
14	14	47	0	31 (87)
15	15	47	0	36 (84)
16	18	47	22	39 (95)
17	19	47	0	42 (89)
18	14	48	-78	32 (70)

<sup>a</sup>Cuprate reagents [C<sub>6</sub>H<sub>5</sub>SCuR]Li: 44, R = Me; 45, R = *n*-Bu; 46, R = *sec*-Bu; 47, R = *i*-Bu; 48, R = CH=CH<sub>2</sub>. Relative to the quantities of β-bromo enones used, the following amounts of reagents were employed: 44, 2.0 equiv. (Entries 1-6); 45-47, 1.5 equiv. (Entries 7-17); 48, 3.0 equiv. (Entry 18). <sup>a</sup> The reaction time was 2.5 h in each case. <sup>c</sup>Yield of distilled product. In some of the experiments, a small amount (generally S(2)) for the reaction product of the experiments.

< 5%) of starting material was recovered. <sup>d</sup> The major product in this case was 2-methyl-3-phenylthio-2-cyclopenten-1-one (49) (see text and Experimental).

addition to the initially formed  $\beta$ -alkyl enone. Thus, the mixed cuprate reagents 44-47 are, in general, excellent reagents for the conversion of  $\beta$ -bromo enones into the corresponding  $\beta$ -alkyl enones.

Although lithium (phenylthio)(methyl)cuprate (44) efficiently transformed the 3-bromo-2-cyclohexen-1-ones 12, 14, and 15-17 into the corresponding  $\beta$ -methyl enones (Entries 1–5), a similar reaction of 44 with the  $\beta$ -bromo cyclopentenone 19 afforded 2,3-dimethyl-2-cyclopenten-1-one (40) in very poor yield (Entry 6). In fact, the major product of this reaction was the crystalline 2-methyl-3-phenylthio-2-cyclopenten-1-one (49), showing that, in this case, phenylthio transfer was more facile than methyl transfer.<sup>4</sup> It was subsequently found, however, that the formation of 49 could be avoided nearly completely by use of the iodo enone 50 in place of the corresponding bromo compound 19. Thus, treatment of 50 with the cuprate reagent 44 afforded 2,3-dimethyl-2-cyclopenten-1-one (40) in high yield.



The reactions involving  $\beta$ -bromo enones and lithium (phenylthio)(tert-butyl)cuprate (47) proved to be remarkably efficient (Entries 13-17). Although the *tert*-butyl enones 27(39), 31(40), and 42(41) had been prepared previously via entirely different synthetic processes, the yields were generally low. In contrast, the present method provided these substances in excellent yields. Furthermore, even the relatively highly hindered  $\beta$ -bromo enones 15, 18, and 19 reacted smoothly with the cuprate reagent 47 to give the corresponding  $\beta$ -tertbutyl enones 36, 39, and 42 in yields greater than 80%.

Treatment of 3-bromo-2-cyclohexen-1-one (14) with 1.3 equiv. of lithium (phenylthio)(vinyl)cuprate (48) in tetrahydrofuran at  $-78^{\circ}$ C gave, in addition to starting material, the  $\alpha,\beta$ -unsaturated ketone 32 (ratio  $\approx$ 7:2, respectively). Clearly, 1,6 addition of the cuprate reagent 48 to the initially formed 3-vinyl-2-cyclohexen-1-one occurred at a rate faster

<sup>&</sup>lt;sup>4</sup>In general, transfer of the C<sub>6</sub>H<sub>5</sub>S group was not a problem in these reactions. Although small amounts of the β-phenylthio cycloalkenones were also formed in the experiments summarized in Entries 2-5 and 10, the yields of the desired  $\beta$ -alkyl enones were quite satisfactory.

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than the original 1,4 addition to 14. Reaction of 14 with 3.0 equiv. of the cuprate reagent 48 provided 32 in 70% yield (Entry 18).

## (c) Synthesis of (Z)-jasmone (53)<sup>5</sup>

From a structural point of view, (Z)-jasmone (53) is a relatively simple compound. However, partly because of the fact that this substance is an important compound in the perfume industry and partly because it serves as a convenient synthetic target for testing new synthetic methods aimed at cyclopentenone-type compounds, (Z)-jasmone (53) has been synthesized many times via many different pathways. Reported here is a simple conversion of 1,3-cyclopentanedione into this natural product.

Alkylation of 1,3-cyclopentanedione with (Z)-1-chloro-2-pentene afforded compound **51** (41%) which, upon treatment with triphenylphosphine dibromide in the presence of triethylamine (35), was transformed smoothly (82%) into the  $\beta$ -bromo enone **52**. When the latter substance was allowed to react with Me<sub>2</sub>CuLi in ether at 0°C, (Z)-jasmone (**53**) was produced in 93% yield.



#### Experimental

#### General

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Melting points, which were taken on a Fisher–Johns melting point apparatus, and distillation temperatures are uncorrected. Infrared (ir) spectra were recorded on a Perkin–Elmer model 710 spectrophotometer. Proton magnetic resonance ('H nmr) spectra (deuterochloroform solution) were measured using Varian Associates spectrometers, models T-60 and/or HA-100 or XL-100. Signal positions are given in  $\delta$  units, with tetramethylsilane as the internal standard. High resolution mass spectrometric measurements were recorded on a Kratos MS-50 mass spectrometer. Gas–liquid chromatography (glc) was carried out with a Hewlett–Packard model 5832A gas chromatograph (analytical) or with a Varian Aerograph model 90-P instrument (preparative). Microanalyses were performed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia, Vancouver, B.C.

## General procedure for the reaction of $\beta$ -halo $\alpha$ , $\beta$ -unsaturated ketones with lithium dimethylcuprate (Table 1)

To a cold  $(-78^{\circ}C)$ , stirred solution of the indicated amount of lithium dimethylcuprate (44) in anhydrous ether ( $\sim 6-10 \text{ mL}$  per

mmol of reagent) under an atmosphere of nitrogen was added a solution of 1.0 mmol of  $\beta$ -halo enone (11–15, 17, 19, 20) in anhydrous ether (~3 mL). After the resulting solution had been stirred at the designated temperature for the required length of time, it was treated with cold (0°C) saturated aqueous ammonium chloride (~5 mL). The resulting mixture was extracted thoroughly with ether. The combined ethereal extract was washed with brine and dried over anhydrous magnesium sulfate. Removal of the solvent, followed by bulb-to-bulb distillation of the residual oil under reduced pressure (water aspirator or vacuum pump), afforded the product(s).

## Table 1, Entries 1-3

The product was 3,3,5,5-tetramethylcyclohexanone (21) (45); ir (film):  $1710 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 1.07 (s, 12H), 1.57 (s, 2H), 2.16 (s, 4H).

#### Table 1, Entry 4

The product was 3,3-dimethylcyclohexanone (22) (46); ir (film):  $1712 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 1.07 (s, 6H), 1.46–2.60 (diffuse, 8H).

#### Table 1, Entry 5

The product was 2,3,3-trimethylcyclohexanone (23) (47); ir (film):  $1710 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 0.79, 1.06 (s, s, 3H each), 0.98 (d, 3H, J = 7 Hz), 1.50–2.53 (diffuse, 7H).

#### Table 2, Entry 6

Analysis of the product by glc indicated the presence of two components, in a ratio of 9:1. The minor component was shown to possess retention times identical with those of the enone **37**, which was prepared via another reaction (*vide infra*). The major component, a pure sample of which was collected by preparative glc, was 2-(2-cyanoethyl)-3,3-dimethylcyclohexanone (**24**); ir (film): 2250, 1705 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 0.77, 1.13 (s, s, 3H each), 1.30–2.63 (diffuse, 11H). *Anal.* calcd. for C<sub>11</sub>H<sub>17</sub>NO: C 73.70, H 9.56, N 7.81; found: C 73.44, H 9.50, N 7.60.

## Table 1, Entry 7

The product was 2,3-dimethyl-2-cyclopenten-1-one (**40**) (48); ir (film): 1700, 1650 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.70 (broad s, 3H), 2.05 (s, 3H), 2.23–2.66 (diffuse, 4H).

#### Table 1, Entry 8

The product was 2-allyl-3-methyl-2-cyclopenten-1-one (43) (49); ir (film): 1700,  $1640 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 2.04 (s, 3H), 2.30–2.66 (m, 4H), 2.84–3.12 (m, 2H), 4.86–5.24 (m, 2H), 5.58–6.04 (m, 1H).

## Table 1, Entries 9 and 10

Analysis of the products from these two experiments showed that in each case the minor product exhibited retention times identical with those of 3,3,5,5-tetramethylcyclohexanone (21). The product mixture from the experiment summarized in Entry 9 also contained a small amount (4%) of the starting material, bromo enone 12. In each case, a sample of the major product was isolated by preparative glc and was shown to be 3,5,5-trimethyl-2-cyclohexen-1-one (25); ir (film): 1673, 1635 cm<sup>-1</sup>; <sup>1</sup>H nmT  $\delta$ : 1.05 (s, 6H), 1.93 (broad s, 3H), 2.20 (broad s, 4H), 5.90 (m, 1H).

## Table 1, Entry 11

Gas-liquid chromatographic analysis showed that the material obtained from this experiment consisted of the starting material 15 and 2,3-dimethyl-2-cyclohexen-1-one (33), a sample of which was collected by preparative glc; ir (film): 1668, 1635 cm<sup>-1</sup>;<sup>1</sup>H nmr  $\delta$ : 1.76 (broad s, 3H), 1.90–2.13 (m, 5H), 2.20–2.60 (m, 4H).

## General procedure for the reaction of β-bromoα, β-unsaturated ketones with lithium (phenylthio)(alkyl)cuprates (Table 2)

To a cold  $(-20^{\circ}C)$  stirred suspension of (phenylthio)copper (38) (for reagent 44, 2 mmol; for reagents 45–47, 1.5 mmol; for reagent 48, 3 mmol) in dry THF (10 mL), under an atmosphere of nitrogen, was added via syringe a required amount of alkyllith-

<sup>&</sup>lt;sup>5</sup>A perusal of the chemical literature makes it abundantly clear that there is no lack of (Z)-jasmone syntheses (see refs. 42 and 43 and citations therein). However, it is difficult to escape the impression that if a person is actively engaged in research in the area of synthetic organic chemistry, then it is "necessary" for him (her) to report at some time during his (her) career a synthesis of this natural product. Described in this brief section of the paper is our (modest) contribution to this area.

ium or vinyllithium solution (methyllithium in ether, 2 mmol; n-butyllithium in hexane, 1.5 mmol; sec-butyllithium in cyclohexane, 1.5 mmol; tert-butyllithium in pentane, 1.5 mmol; vinyllithium in THF, 3 mmol).6 The resultant mixture was stirred at -20°C for 15 min and then was cooled to -78°C. A solution of the appropriate  $\beta$ -bromo enone (1 mmol) in 2 mL of THF was added and the reaction mixture was stirred at the indicated temperature for 2.5 h. Methanol (1 mL), saturated aqueous ammonium chloride (0.5 mL), ether (10 mL), and anhydrous magnesium sulfate (4g) were added sequentially, the resultant mixture was stirred for a few minutes and then was filtered through a short column of silica gel ( $\sim 10-15$  g). The column was eluted with  $\sim 100 \,\text{mL}$  of ether. Removal of the solvent from the combined eluate, followed by bulb-to-bulb distillation of the residual oil under reduced pressure (water aspirator), afforded the product. In some of the experiments, gas-liquid chromatographic analysis of the product indicated the presence of a small amount ( $\leq 5\%$ ) of starting material. In each of these cases, a pure sample of the desired  $\beta$ -alkyl enone was obtained by preparative glc

## Table 2, Entry 1

The product was 3,5,5-trimethyl-2-cyclohexen-1-one (25) (vide supra).

Table 2, Entry 2

The product was 3-methyl-2-cyclohexen-1-one (**28**); ir (film): 1665, 1630 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.76–2.57 (diffuse, 6H), 1.97 (s, 3H), 5.87 (m, 1H).

Table 2, Entry 3

The product was 2,3-dimethyl-2-cyclohexen-1-one (33) (vide supra).

Table 2, Entry 4

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The product was 2-allyl-3-methyl-2-cyclohexen-1-one (**37**) (52); ir (film): 1665, 1630, 985, 895 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.80–2.17 (diffuse, 2H), 1.95 (s, 3H), 2.23–2.60 (m, 4H), 3.08 (broad d, 2H, J = 6 Hz), 4.72–5.20 (m, 2H), 5.44–6.17 (m, 1H).

## Table 2, Entry 5

The product was 2-(2-cyanoethyl)-3-methyl-2-cyclohexen-1one (**38**); ir (film): 2255, 1662, 1628 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.78–2.15 (diffuse, 2H), 2.05 (s, 3H), 2.22–2.66 (diffuse, 8H). *Anal.* calcd. for C<sub>10</sub>H<sub>13</sub>NO: C 73.59, H 8.02, N 8.57; found: C 73.25, H 8.15, N 8.29.

#### Table 2, Entry 6

The volatile product was 2,3-dimethyl-2-cyclopenten-1-one (40) (*vide supra*). The residue from the distillation was purified by column chromatography on silica gel. Recrystallization (ether) of the solid thus obtained gave 2-methyl-3-phenylthio-2-cyclopenten-1-one (49) (61%), mp 96–98°C; ir (CHCl<sub>3</sub>): 1675, 1595 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.87 (broad s, 3H), 2.36 (broad s, 4H), 7.33–7.70 (diffuse, 5H). *Anal.* calcd. for C<sub>12</sub>H<sub>12</sub>OS: C 70.54, H 5.92; found: C 70.25, H 6.00.

#### Table 2, Entry 7

The product was 3-*n*-butyl-5,5-dimethyl-2-cyclohexen-1-one (26) (52); ir (film): 1670, 1630 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.03 (poorly resolved t, 3H), 1.17 (s, 6H), 1.23–1.86 (diffuse, 4H), 2.04–2.53 (diffuse, 6H), 6.02 (broad s, 1H).

#### Table 2, Entry 8

The product was 3-*n*-butyl-2-cyclohexen-1-one (**29**) (52); ir (film): 1670, 1625 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 0.90 (poorly resolved t, 3H), 1.13–1.63 (diffuse, 6H), 1.70–2.70 (diffuse, 6H), 5.87 (m, 1H).

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Table 2, Entry 9

The product was 3-*n*-butyl-2-methyl-2-cyclohexen-1-one (**34**); ir (film): 1670, 1627 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 0.98 (poorly resolved t, 3H), 1.10–1.66 (diffuse, 6H), 1.70–2.63 (diffuse, 6H), 1.83 (t, 3H,  $J \approx$ 1 Hz). Anal. calcd. for C<sub>11</sub>H<sub>18</sub>O: C 79.52, H 10.91; found: C 79.52, H 10.96.

#### Table 2, Entry 10

The product was 3-*n*-butyl-2-methyl-2-cyclopenten-1-one (**41**) (53); ir (film): 1705,  $1645 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 1.13 (poorly resolved t, 3H), 1.33-1.84 (diffuse, 4H), 1.88 (s, 3H), 2.40-2.87 (unresolved m, 6H).

#### Table 2, Entry 11

The product was 3-*sec*-butyl-2-cyclohexen-1-one (**30**) (54); ir (film): 1665, 1620 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.01 (t, 3H, J = 6 Hz), 1.25 (d, 3H, J = 7 Hz), 1.33–2.70 (diffuse, 9H), 6.02 (s, 1H).

#### Table 2, Entry 12

The product was 3-sec-butyl-2-methyl-2-cyclohexen-1-one (35); ir (film): 1667, 1618 cm<sup>-1</sup>; <sup>1</sup>H nmr & 0.86 (t, 3H, J = 7 Hz), 1.04 (d, 3H, J = 7 Hz), 1.46 (quintet, 2H, J = 7 Hz), 1.74–2.06 (m, 2H), 1.80 (t, 3H, J = 2 Hz), 2.16–2.52 (m, 4H), 2.81 (hextet, 1H, J = 7 Hz). *Exact Mass* calcd. for C<sub>11</sub>H<sub>18</sub>O: 166.1357; found: 166.1380.

#### Table 2, Entry 13

The product was 3-*tert*-butyl-5,5-dimethyl-2-cyclohexen-1one (27) (39); ir (film): 1672,  $1618 \text{ cm}^{-1}$ ; <sup>1</sup>H nmr  $\delta$ : 1.03 (s, 6H), 1.12 (s, 9H), 2.20 (broad s, 4H), 5.97 (broad s, 1H).

#### Table 2, Entry 14

The product was 3-*tert*-butyl-2-cyclohexen-1-one (**31**) (40); ir (film): 1667, 1613 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.13 (s, 9H), 1.65–2.53 (diffuse, 6H), 5.97 (broad s, 1H).

## Table 2, Entry 15

The product was 3-*tert*-butyl-2-methyl-2-cyclohexen-1-one (36); ir (film): 1665, 1592 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.26 (s, 9H), 1.70–2.10 (diffuse, 2H), 1.93 (t, 3H, J = 2Hz), 2.12–2.58 (diffuse, 4H). Anal. calcd. for C<sub>11</sub>H<sub>18</sub>O: C 79.52, H 10.91; found: C 79.77, H 10.85.

#### Table 2, Entry 16

The product was 3-*tert*-butyl-2,5,5-trimethyl-2-cyclohexen-1-one (**39**); ir (film): 1662, 1596 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 0.99 (s, 6H), 1.26 (s, 9H), 1.96 (t, 3H,  $J \approx 2$  Hz), 2.20 (s, 2H), 2.28 (q, 2H,  $J \approx$ 2 Hz). Anal. calcd. for C<sub>13</sub>H<sub>22</sub>O: C 80.35, H 11.35; found: C 80.45, H 11.31.

#### Table 2, Entry 17

The product was 3-*tert*-butyl-2-methyl-2-cyclopenten-1-one (42) (41); ir (film): 1695, 1640 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.26 (s, 9H), 1.84 (t, 3H,  $J \approx 2$  Hz), 2.17–2.70 (diffuse, 4H).

#### Table 2, Entry 18

The product was 3-(3-butenyl)-2-cyclohexen-1-one (**32**) (55); ir (film): 1670, 1625, 980, 895 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 1.75–2.80 (diffuse, 10H), 4.84–5.27 (diffuse, 2H), 5.44–6.06 (diffuse, 1H), 5.91 (broad s, 1H).

## Reaction of 3-iodo-2-methyl-2-cyclopenten-1-one (50) with lithium (phenylthio)(methyl)cuprate (44)

To a cold  $(-20^{\circ}\text{C})$  stirred solution of the cuprate reagent 44 (2 mmol) in dry THF (10 mL), under an atmosphere of nitrogen, was added a solution of the iodo enone 50 (222 mg, 1.0 mmol) in 2 mL of THF. The reaction mixture was allowed to warm to 0°C and was stirred at this temperature for 2.5 h. Subjection of the reaction mixture to work-up as described above, followed by distillation (air-bath temperature 65–75°C/21 Torr) of the crude product, gave 100 mg (91%) of 2,3-dimethyl-2-cyclopenten-1-one (40) (vide supra).

#### 2- [(Z)-2-Pentenyl]-1,3-cyclopentanedione (51)

To an ice-cold solution of 1,3-cyclopentanedione (750 mg,

<sup>&</sup>lt;sup>6</sup>The solutions of the alkyllithium reagents were purchased from the Alfa Division of Ventron Corporation, while vinyllithium in THF was prepared by the procedure of Seyferth and Weiner (50). These reagents were standardized by the method of Gilman and Cartledge (51).

7.5 mmol) in 2 M aqueous potassium hydroxide (4 mL, 8 mmol) was added (Z)-1-chloro-2-pentene (885 mg, 8.5 mmol) and a small amount of copper powder. The reaction mixture was stirred at 0°C for 1 h and then at room temperature for 3.5 h. The reaction mixture was made alkaline by addition of 10% aqueous sodium hydroxide and the resultant solution was washed with ether, cooled to 0°C, and acidified by addition of 3 N hydrochloric acid. The resulting mixture was extracted thoroughly with chloroform. The combined extracts were dried over anhydrous magnesium sulfate. Removal of the solvent gave a yellow oil which, upon crystallization from ether, afforded 510 mg (41%) of 2-[(Z)-2-pentenyl]-1,3-cyclopentanedione (51), mp 135-136°C; <sup>1</sup>H nmr  $\delta$ : 0.92 (t, 3H, J = 7.5 Hz), 2.15 (m, 2H), 2.52 (s, 4H), 2.94 (broad d, 2H, J = 6.0 Hz), 5.36–5.54 (m, 2H), 8.62 (broad s, 1H). The <sup>1</sup>H nmr spectrum clearly indicated that this compound existed very largely in the enol tautomer. Anal. calcd. for C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>: C 72.26, H 8.49; found: C 72.06, H 8.45.

## 3-Bromo-2-[(Z)-2-pentenyl]-2-cyclopenten-1-one (52)

To an ice-cold, stirred solution of triphenylphosphine (435 mg, 1.66 mmol) in benzene (10 mL) was added, dropwise, a 1 M solution of bromine in dry benzene (1.66 mL, 1.66 mmol). To the resulting suspension was added triethylamine (167 mg, 1.66 mmol) and a solution of 2-[(Z)-2-penteny]-1, 3-cyclopentanedione (51)(250 mg, 1.5 mmol) in benzene (8 mL). The reaction mixture was stirred at room temperature for 4h and was then diluted with 100 mL of ether. The resulting mixture (suspension) was filtered through a short column of neutral, activity II, silica gel. The column was eluted with an additional 200 mL of ether. Removal of the solvent from the combined eluate, followed by distillation (air-bath temperature 105-115°C/0.5 Torr) of the residual oil gave 283 mg (82%) of 3-bromo-2-[(Z)-2-pentenyl]-2-cyclopenten-1-one (52) as a clear colorless oil; ir (film): 1700, 1625, 1300, 1195 cm<sup>-1</sup>; <sup>1</sup>H nmr  $\delta$ : 0.98 (t, 3H, J = 7.5 Hz), 2.18 (m, 2H), 2.52 (m, 2H), 2.82-3.10 (m, 4H), 5.10-5.62 (m, 2H). Anal. calcd. for C<sub>10</sub>H<sub>13</sub>BrO: C 52.41, H 5.73, Br 34.87; found: C 52.16, H 5.55, Br 34.70.

## (Z)-Jasmone (53)

To a cold  $(-78^{\circ}\text{C})$  stirred solution of lithium dimethylcuprate (1.15 mmol) in anhydrous ether (8 mL), under an atmosphere of nitrogen, was added over a period of 10 min a solution of 3-bromo-2-[(Z)-2-pentenyl]-2-cyclopenten-1-one (52) (120 mg, 0.52 mmol) in ether (2 mL). The reaction mixture was allowed to warm to 0°C and was stirred at 0°C for 1 h. Saturated aqueous ammonium chloride was added and the resulting mixture was thoroughly extracted with ether. The combined extracts were dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure afforded 80 mg (93%) of pure (Z)-jasmone (53) as a pale yellow oil; ir (film): 1685, 1640, 1440, 1380, 1340, 1300, 1175, 1070 cm<sup>-1</sup>; <sup>1</sup>H nmr & 0.98 (t, 3H, J = 7.5 Hz), 2.06 (s, 3H), 2.02–2.28 (m, 2H), 2.30–2.70 (m, 4H), 2.95 (d, 2H, J = 6.0 Hz), 5.10–5.56 (m, 2H).

#### Acknowledgements

Financial support for this work from the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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