

New Functionalized Cycloheptatrienes *via* Tropone σ -Adducts

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We report that, on treatment with phenyl-lithium, followed by triethyloxonium tetrafluoroborate in diethyl ether at -78°C , (i) 2-chloro- and 2-bromo-tropone give the corresponding 1-ethoxy-2-halogeno-7-phenylcycloheptatriene; (ii) 2-fluorotropone gives 2-ethoxy-3,7-diphenylcycloheptatriene; and (iii) tropone affords 1-ethoxy-2-phenylcycloheptatriene. Conceivably, in case (i) the tropone undergoes phenyl-lithium attack at C-7, followed by *O*-alkylation of the enolate, while in case (iii) the intermediate enolate suffers base-catalysed rearrangement and, finally, in case (iii) nucleophilic replacement of fluorine by phenyl-lithium from the tropone precedes phenyl-lithium attack at C-7 of the resulting 2-phenyltropone. This gives a better synthesis, than those available so far, of 2-chloro-7-aryltropones; in addition, a 1-alkoxy-2-chloro-7-phenylcycloheptatriene undergoes selenium dioxide oxidation to 2-chloro-7-phenyltropone.

Cycloheptatrienes, owing to a variety of possible ring transformations, are potentially useful intermediates in organic synthesis. This requires, however, that suitably functionalized cycloheptatrienes are made easily available. Besides other laboratories,¹ our own has contributed to the progress in this field in recent years.²

We now report on the reactions of cycloheptatrienes carrying halogen or/and alkoxy substituents. These were prepared by adding an aryl-lithium reagent to a tropone and trapping the resulting enolate with an electrophile.

The results in the Table show that 2-chloro- (1), 2-chloro-[3,5,7- $^2\text{H}_3$] (2), and 2-bromo-tropone (3), when the electrophile is either the Meerwein reagent or trimethylchlorosilane, give the corresponding 1-alkoxy- (7)–(9) or 1-trimethylsiloxy-2-halogeno-7-phenylcycloheptatriene (11). The only difference, in the two cases, is that while the chloro compounds (7) and (8) proved to be quite stable, the bromo compound (9) was labile. 2-Phenyltropone (4) shows similar behaviour, giving a 1-alkoxy-2,7-diphenylcycloheptatriene (10).

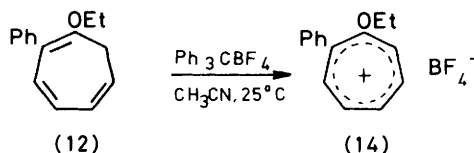
2-Fluorotropone (5) shows different behaviour, giving the same product (10) as obtained from the reaction of 2-phenyltropone.

The case of tropone (6) is different again. In fact, tropone, under the above conditions, gave mainly 1-alkoxy-2-phenylcycloheptatrienes (12) and (13), which were accompanied by their decomposition products (of uncertain structure) and, in the case of the reaction with trimethyloxonium tetrafluoroborate, also by the isomeric 1-methoxy-7-phenylcycloheptatriene. H.p.l.c. served to isolate these products.

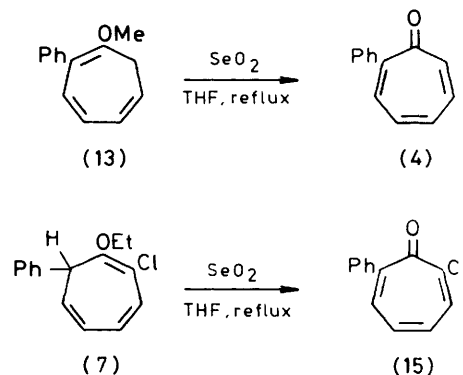
The assigned structures of the above products rest mainly on spectra and on some chemical considerations. As regards the products of the first type, (7)–(9) and (11), mass spectra showed an intense molecular ion and logical fragments. The ^1H n.m.r. spectra revealed 7-H, at the expected chemical shifts,² as a doublet (coupled with 6-H), while 4-H could be identified through the deuterated analogue (8).

With the products from tropone, (12) and (13), which gave the molecular ion as base peak, no ^1H n.m.r. resonance for a geminal CHPh proton at the saturated cycloheptatriene carbon² could be detected. A cycloheptatriene methylene was observed instead, as a doublet. This is only compatible with the cycloheptatriene methylene being close to either the alkoxy or phenyl-bearing carbon. The first possibility, (12) and (13), was unequivocally shown to be correct by the effects of added $\text{Eu}(\text{fod})_3$ † which, for example in the case of (12), induced a

low-field shift of the resonances only for OCH_2 (11.0), CH_3 (6.7), *ortho* phenyl protons (5.7), and 7- H_2 (4.6 Hz), while the multiplet for 3-H remained unchanged. The ^{13}C n.m.r. spectrum for (12) further supports these conclusions, showing $\text{Eu}(\text{fod})_3$ -induced low-field shifts of resonances only for C(1) (7.9), OCH_2 (8.8), C-7 (5.0), C-2 (4.8), and CH_3 (4.0 Hz). In agreement with the proposed structure, treatment of (12) with trityl (triphenylmethyl) tetrafluoroborate led to the tropylium ion (14).‡



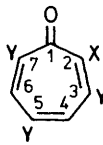
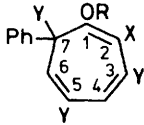
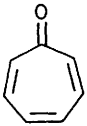
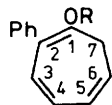
Let us now digress briefly about the behaviour of (13) or (7) towards selenium dioxide in tetrahydrofuran (THF). We observed the formation of either 2-phenyltropone (4) or 2-chloro-7-phenyltropone (15) from, respectively, (13) or (7).



‡ On treatment with trityl perchlorate in acetonitrile at 25°C , compound (7) was recovered unchanged. More drastic conditions, as in the case of other 7-phenylcycloheptatrienes (C. Jutz and F. Voithenleitner, *Chem. Ber.*, 1964, **97**, 29), were not attempted in order to avoid thermally induced sigmatropic hydrogen shifts. Compound (10), under similar conditions, was degraded and no tropylium salt could be isolated.

† $\text{Eu}(\text{fod})_3$ = Europium tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-octane-3,5-dionate).

Table. Reactions of tropones with phenyl-lithium, followed by $R_3\text{OBF}_4$ in diethyl ether at -78°C

Substrate	Electrophile	Product (yield %)
		
(1) X = Cl, Y = H	Et_3OBF_4	(7) X = Cl, R = Et, Y = H (45)
(2) X = Cl, Y = D	Et_3OBF_4	(8) X = Cl, R = Et, Y = D (44)
(3) X = Br, Y = H	Et_3OBF_4	(9) X = Br, R = Et, Y = H (14) ^a
(4) X = Ph, Y = H	Et_3OBF_4	(10) X = Ph, R = Et, Y = H (61)
(5) X = F, Y = H	Et_3OBF_4	(10) X = Ph, R = Et, Y = H (25) ^b
(1) X = Cl, Y = H	Me_3SiCl	(11) X = Cl, R = SiMe ₃ , Y = H (38)
	$\left\{ \begin{array}{l} \text{Et}_3\text{OBF}_4 \\ \text{Me}_3\text{OBF}_4 \end{array} \right.$	
(6) X = Y = H		(12) R = Et (30) ^c (13) R = Me (30) ^c

^a The low yield is due to the instability of (9), which decomposed extensively during isolation. ^b The low yield is due to the use of only 1.2 mol equiv. of PhLi. ^c Yield after repeated h.p.l.c. purification.

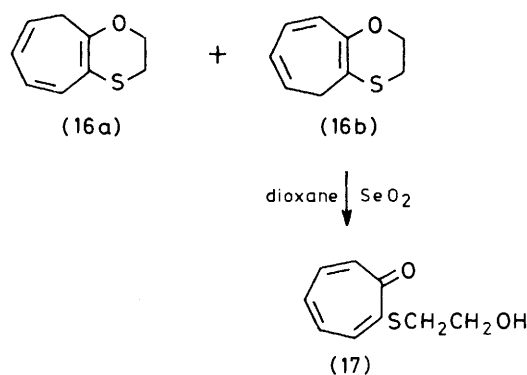
Although the yields were poor (*ca.* 25%) these reactions, which are clearly reminiscent of the selenium dioxide oxidation of the mixture of (16a) and (16b) to give (17) which we recently reported,^{2b} have some interest. In fact, the only reported alternative synthesis of tropones carrying a halogen and an aryl group at the α, α' -positions requires, just as in the case of (15),³ treatment of tropolone with phenyl-lithium to obtain 2-phenyltropolone.⁴ The latter was brominated to 2-bromo-7-phenyltropolone which was then hydrolysed in aqueous hydrogen bromide to 3-phenyltropolone.⁴ Chlorination of the latter with either thionyl chloride^{3a} or hydrogen chloride– CuSO_4 ^{3b} gave a mixture of 2-chloro-7- and 2-chloro-3-phenyltropolone which had to be separated by chromatography.^{3a} Our synthesis of (15), which could easily be extended

2-phenyltropolone rests on ¹H n.m.r. spectra which showed the 7- and 6-H protons at much the same frequency, and with the same couplings, as with the corresponding protons of species (7) and (9).

Formation of compounds (7)–(11) (Table) is easily accounted for. As regards (7)–(9) and (11), we reason that the respective starting substrate undergoes phenyl-lithium addition at C-7 and that the resulting enolate undergoes either *O*-alkylation or *O*-trimethylsilylation. This is in line with the recognized activation by the halogen of the troponone ring for nucleophilic attack. Probably, concomitant steric hindrance by the halogen for nucleophilic attack at C-2 also plays a role.⁵

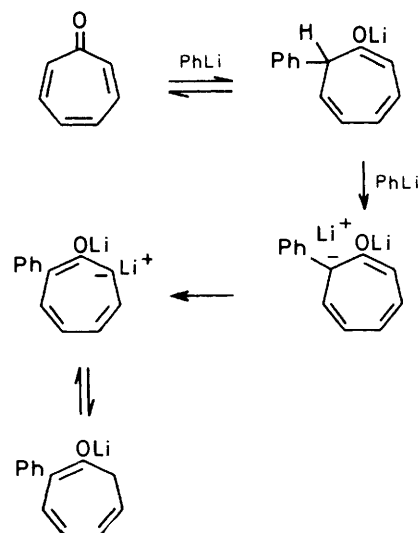
In the case of 2-fluorotropolone (5), which gives (10) (Table), fluorine replacement by phenyl-lithium occurs first, followed by phenyl-lithium addition at C-7. The latter reaction was in fact directly proved (4) \rightarrow (10) (Table).

It is more difficult to account for the formation of com-



to other related cases, does not involve the separation of isomers* and is quicker than previous syntheses.^{3,4}

Returning to the main theme of cycloheptatrienes, structure (10) for the product obtained from either fluorotropolone or



Scheme.

* Of course, in the case of an unsymmetrically substituted troponone, our synthesis would require the separation of isomers (the substituted 2-chlorotropolones resulting from chlorination of the substituted troponone).

pounds (12) and (13). We propose that the enolate generated by phenyl-lithium attack at the tropone α -carbon undergoes base-catalysed isomerization, *via* the doubly negatively charged carbanions depicted in the Scheme, to give a new enolate from which (12) or (13) are finally derived during the work-up.

Base-catalysed hydrogen shifts around the 7-phenylcycloheptatriene ring have ample precedent.^{1b} However, our reactions, as depicted in the Scheme, are peculiar in requiring doubly negatively charged species.

Thermal, sigmatropic hydrogen shifts, being known to require much higher temperatures than in our experiments,^{1b} are unable to account for the rearrangement we have observed here. In fact, while both (12) and (13) were able to undergo spontaneous, ready degradation, even at low temperature, under neutral conditions, to give products lacking either 7-H₂ or 7-HPH cycloheptatriene groupings, the isomeric 1-methoxy-7-phenylcycloheptatriene proved to be quite stable under the same conditions.

In conclusion, we have provided here an easy entry to new 1,2-difunctionalized cycloheptatrienes which may prove useful in the context set forth at the beginning of this paper.

Experimental

General directions are given in the text. Preparative t.l.c. (p.l.c.) was carried out on Merck Kieselgel 60 P₂₅₄, 2-mm thick silica gel plates, developer n-hexane unless otherwise stated. H.p.l.c. was carried out on a Merck LiChrosorb Si 60, 7- μ m column, eluant n-hexane, flow rate 5 ml min⁻¹. N.m.r. spectra were run on Varian spectrometers (¹H at 80 MHz on a modified model CFT20 and 60 MHz on a model 360; ¹³C at 20 MHz on a model CFT20); δ values are given in p.p.m. with respect to internal tetramethylsilane as internal standard. Electron-impact mass spectra were taken with a Hewlett-Packard model 5995A.

2-Chloro-1-ethoxy-7-phenylcycloheptatriene (7).—Phenyl-lithium (3.7 mmol) was added, as a 2.3M solution in benzene-diethyl ether, to a stirred solution of 2-chlorotropone (1) (0.43 g, 3.1 mmol) in ethyl ether (30 ml) at -78°C under nitrogen. After 30 min triethyloxonium tetrafluoroborate (1.1 g) was added and the mixture was held at 0°C overnight. Then water (15 ml) was added and the organic layer was separated while the aqueous layer was washed with diethyl ether. The combined organic layers were dried over Na₂SO₄ and then evaporated at reduced pressure, never allowing the temperature to rise above $35\text{--}40^\circ\text{C}$. The residue was subjected to p.l.c., and the band with R_F 0.56 was collected, from which oily compound (7) (0.225 g, 45%) was obtained (Found: C, 73.0; H, 6.1. C₁₅H₁₅ClO requires C, 73.02; H, 6.13%); m/z 248 (9%, $M + 2$), 246 (28, M), 217 (19, $M - \text{C}_2\text{H}_5$), 211 (33, $M - \text{Cl}$), and 183 (100); $\delta(\text{C}_6\text{D}_6$; 80 MHz) 7.1 (5 H, m, Ph), 6.3–6.0 (3 H, m, 3-, 4-, and 5-H), 5.5 (1 H, m, 6-H), 3.76 (1 H, d, $J_{7,6}$ 8.8 Hz, 7-H), 3.66 (2 H, q, J 7.0 Hz, CH₂), and 0.97 (3 H, t, J 7.0 Hz, CH₃); on irradiation at δ 5.5 the doublet at δ 3.76 became a singlet; $\delta(\text{CDCl}_3$; 80 MHz) 7.2 (5 H, m, Ph), 6.3 (3 H, m, 3-, 4-, and 5-H), 5.8 (1 H, m, 6-H), 3.9 (3 H, superimposed q for CH₂ and d for 7-H), and 1.18 (3 H, t, J 6.9 Hz, CH₃); on irradiation at δ 5.8, a quartet for CH₂, with a singlet for 7-H in the centre, was observed.

2-Chloro-1-ethoxy-7-phenyl[3,5,7-²H₃]cycloheptatriene (8).—Similarly, compound (2) gave oily (8), R_F 0.56 (44% yield); m/z 251 (9%, $M + 2$), 249 (28, M), 220 (19, $M - \text{C}_2\text{H}_5$), 214 (32, $M - \text{Cl}$), and 186 (100); $\delta(\text{CDCl}_3$; 60 MHz) 7.1

(15 H, m, Ph), 6.2 (1 H, br s, 4-H), 5.7 (1 H, br s, 6-H), 3.70 (2 H, q, J 7.0 Hz, CH₂), and 1.0 (3 H, t, J 7.0 Hz, CH₃).

2-Bromo-1-ethoxy-7-phenylcycloheptatriene (9).—Similarly, compound (3) gave oily compound (9) in poor yield (14%, see text), R_F 0.7 (Found: C, 62.0; H, 5.15. C₁₅H₁₅BrO requires C, 61.87; H, 5.19%); $\delta(\text{CDCl}_3$; 60 MHz) 7.1 (5 H, m, Ph), 6.4–6.0 (3 H, m, 3-, 4-, and 5-H), 5.7 (1 H, m, 6-H), 3.9 (1 H, d, $J_{7,6}$ 8.0 Hz, 7-H), 3.78 (2 H, q, J 7.0 Hz, CH₂), and 1.15 (3 H, t, J 7.0 Hz, CH₃); on irradiation at δ 5.7, the δ 3.9 doublet became a singlet.

2-Chloro-7-phenyl-1-trimethylsilyloxycycloheptatriene (11).—Phenyl-lithium (1.9 mmol) was added, as a 2.3M benzene-diethyl ether solution, to a stirred solution of 2-chlorotropone (1) (0.25 g, 1.8 mmol) in diethyl ether (10 ml) at -78°C under nitrogen. After 20 min Me₃SiCl (0.206 g, 1.9 mmol) was added. On raising the temperature to 0°C , lithium chloride precipitated out. The mixture was rapidly filtered and the filtrate was evaporated under reduced pressure at 0°C to leave compound (11) as an unstable oil (0.2 g, 38%), $\delta(\text{CDCl}_3$; 60 MHz) 7.1 (5 H, m, Ph), 6.3–5.9 (3 H, m, 3-, 4-, and 5-H), 5.6 (1 H, m, 6-H), 3.5 (1 H, d, $J_{7,6}$ 7.2 Hz, 7-H), and 0.0 (9 H, s, SiMe₃). On irradiation at δ 5.6, the δ 3.5 doublet became a singlet.

1-Ethoxy-2,7-diphenylcycloheptatriene (10).—(a) From 2-phenyltropone. In the usual manner, compound (4) gave an oily product (10), R_F 0.6 (61% yield) (Found: C, 87.5; H, 6.9. C₂₁H₂₀O requires C, 87.46; H, 6.99%); $\delta(\text{CDCl}_3$; 60 MHz) 7.2 (10 H, m, 2 \times Ph), 6.5–6.2 (3 H, m, 3-, 4-, and 5-H), 5.7 (1 H, m, 6-H), 3.5 (1 H, d, $J_{7,6}$ 7.2 Hz, 7-H), 3.4 (2 H, q, J 7.0 Hz, CH₂), and 0.9 (3 H, t, J 7.0 Hz, CH₃); on irradiation at δ 5.7, the δ 3.5 doublet became a singlet.

(b) From 2-fluorotropone (5). Similarly, compound (5) gave (10) in 25% yield. The low yield was due to having used only 1.2 mol equiv. of phenyl-lithium.

1-Ethoxy-2-phenylcycloheptatriene (12).—Starting from tropone (6) and phenyl-lithium, addition of Et₃OBF₄ and work-up as described above for the preparation of (7) gave an oily mixture, R_F 0.6, which was subjected to h.p.l.c. (eluant monitored at λ 254 nm). The eluates at 17 and 20 min were collected and gave single peaks in a 1:3 ratio, the second peak corresponding to oily (12) (30%), m/z 212 (100%, M), 211 (18, $M - 1$), 197 (7, $M - \text{CH}_3$), 183 (88, $M - \text{C}_2\text{H}_5$), 167 (32, $M - \text{OC}_2\text{H}_5$), 155 (66, $M - \text{C}_2\text{H}_5 - \text{CO}$), 135 (4, $M - \text{C}_6\text{H}_5$), 91 (16, C₇H₇), and 77 (39, C₆H₅); $\delta(\text{C}_6\text{D}_6$; 80 MHz) 7.46 (2 H, dd, J_{ortho} 8.2, J_{meta} 1.6 Hz, *ortho* phenyl protons), 7.2 (3 H, m, *meta* and *para* phenyl protons), 6.7–6.2 (3 H, m, 3-, 4-, and 5-H), 5.25 (1 H, tdd, $J_{6,7}$ 7.1, $J_{6,5}$ 8.5, $J_{6,4}$ 0.7 Hz, 6-H), 3.41 (2 H, q, J 7.0 Hz, OCH₂), 2.49 (2 H, d, J 7.1 Hz, 7-H₂), and 0.82 (3 H, t, J 7.0 Hz, CH₃); δ_c (C₆D₆) 143.7 (C-1), 140.1 (C-2), 67.4 (OCH₂), 32.1 (C-7), and 15.0 p.p.m. (CH₃), while phenyl resonances were obscured by those of the solvent and the other resonances were difficult to assign because of the rapid deterioration of compound (12) which caused spurious resonances.

1-Ethoxy-2-phenyltropylium Tetrafluoroborate (14).—To a solution of triphenylmethyl tetrafluoroborate (0.311 g, 0.94 mmol) in dry acetonitrile (2 ml) was added, under nitrogen, a solution of (12) (0.2 g, 0.94 mmol) in dry acetonitrile (1 ml). After 10 min, dry benzene (50 ml) was added, whereby colourless crystals of the tropylium salt (14) separated out. These were filtered off, washed with dry benzene, and dried (0.260 g, 93%), m.p. $138\text{--}139^\circ\text{C}$ (from benzene) (Found: C, 60.4; H, 5.0. C₁₅H₁₅BF₄O requires C, 60.44; H, 5.07%);

$\delta(\text{CD}_3\text{CN}; 60 \text{ MHz})$ 8.2 (5 H, m, tropylium ring protons), 7.1 (5 H, m, Ph), 4.3 (2 H, q, J 7.0 Hz, CH_2), and 1.1 (3 H, t, J 7.0 Hz, CH_3).

1-Methoxy-2-phenylcycloheptatriene (13).—Starting from tropone (6) and phenyl-lithium, addition of Me_3OBF_4 , followed by work-up as described above for the preparation of (7), gave an oily mixture, R_F 0.55, which was subjected to h.p.l.c. (eluant monitored at λ 254 nm). The eluates at 12.5, 15.0, and 18.0 min were collected, and showed single peaks in the proportions 1 : 4 : 1. The eluate at 15.0 min, on evaporation, gave the *title compound* (13) as an oil (30%) (Found: C, 84.9; H, 7.1. $\text{C}_{14}\text{H}_{14}\text{O}$ requires C, 84.81; H, 7.12); m/z 198 (100%, M), 197 (37, $M - 1$), 183 (46, $M - \text{CH}_3$), 182 [13, $M - (\text{H} + \text{CH}_3)$], 167 (40, $M - \text{OCH}_3$), 155 (25, $M - \text{CH}_3 - \text{CO}$), 121 (18, $M - \text{C}_6\text{H}_5$), 91 (25, C_7H_7), and 77 (35, C_6H_5); $\delta(\text{C}_6\text{H}_6; 80 \text{ MHz})$ 7.42 (2 H, dd, J_{ortho} 8.2, J_{meta} 1.7 Hz, *ortho* phenyl protons), 7.1 (3 H, m, *meta* and *para* phenyl protons), 6.6–6.1 (3 H, m, 3-, 4-, and 5-H), 5.22 (1 H, tdd, $J_{6,7}$ 7.1, $J_{6,5}$ 8.3, $J_{6,4}$ 0.8 Hz, 6-H), 3.09 (3 H, s, CH_3), and 2.45 (2 H, d, J 7.1 Hz, 7-H₂). On addition of $\text{Eu}(\text{fod})_3$, only the following resonances were observed to shift: CH_3 (+17.2 Hz), *ortho* phenyl protons (+6.0 Hz), and 7-H₂ (+5.5 Hz), while the multiplet for 3-H did not change at all.

Whilst the eluate at 18 min was shown by n.m.r. to be a complex mixture, the eluate at 12.5 min gave an ^1H n.m.r. spectrum consistent with the structure of 1-methoxy-7-phenylcycloheptatriene: $\delta(\text{C}_6\text{D}_6; 80 \text{ Mz})$ 7.4–7.0 (5 H, m, Ph), 6.4–6.2 (3 H, m, 3-, 4-, and 5-H), 5.53 (1 H, ddd, $J_{6,7}$ 7.8, $J_{6,5}$ 10.0, $J_{6,4}$ 1.7 Hz, 6-H), 5.26 (1 H, dd, $J_{2,3}$ 7.0, $J_{2,4}$ 1.7 Hz, 2-H), 4.02 (1 H, d, J 7.8 Hz, 7-H), and 3.09 (3 H, s, CH_3).

Selenium Dioxide Oxidation of 1-Methoxy-2-phenylcycloheptatriene (13).—To a solution of (13) (0.2 g, 1 mmol) in dry THF (5 ml) was added SeO_2 (0.167 g, 1.5 mmol). The mixture was refluxed for 40 min, whereupon it darkened while a dark red solid separated out. The mixture was filtered and the filtrate was evaporated under reduced pressure to give a

residue which was subjected to p.l.c. [developer benzene–ethanol (4 : 1)]. The band at R_F 0.50 was extracted with chloroform to give 2-phenyltropone (4) (0.130 g, 71%), which proved to be identical in all respects with an authentic sample of 2-phenyltropone.

Selenium Dioxide Oxidation of 2-Chloro-1-ethoxy-7-phenylcycloheptatriene (7).—To a solution of (7) (0.111 g, 0.45 mmol) in dry THF was added SeO_2 (0.54 mmol) and the mixture was refluxed for 50 min. The mixture was then worked up as in the previous reaction and the residue was subjected to p.l.c. with benzene–ethanol (4 : 1) as developer. From the R_F 0.7 band, 2-chloro-7-phenyltropone (15) was obtained as pale yellow prisms (0.025 g, 26%), m.p. 73–75 °C (from ethanol) (lit.,^{3a} 75 °C); m/z 218 (17%, $M + 2$), 217 (40, $M + 1$), 216 (57, M), 215 (100, $M - 1$), and 188 (20, $M - \text{CO}$).

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