# Thermolysis of Phenyl 3-Guaiazulenecarboxylate and the *p*-Acetyl and *p*-Methoxy Derivatives[1)]

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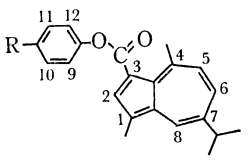
Thermolysis of *p*-acetylphenyl 3-guaiazulenecarboxylate (**1**) results in loss of the ester group. In contrast, thermolysis of phenyl 3-guaiazulenecarboxylate (**2**) or *p*-methoxyphenyl 3-guaiazulenecarboxylate (**3**) gives (i) loss of the ester group, (ii) loss of the 1-methyl group with concomitant rearrangement of the ester group to the 1-position, (iii) interchange of the ester and 1-methyl groups, and (iv) cyclization to 5-isopropyl-7-methyl-1,2-dihydrocyclopenta[*c*,*d*]azulen-1-one (**9**).

Previous studies[2-5)] showed that thermolysis of 3-acylguaiazulenes at 200—260 °C resulted in loss of the acyl group, migration of the acyl group to the 2-position, and/or interchange of the acyl and the 1-methyl groups. It was observed that the nature of the acyl substituent determined the course of the reaction. Thus formyl gave deacylation, acetyl and benzoyl gave migration, and methoxycarbonyl gave acyl-methyl interchange as the main reactions. The mode of reaction in these cases varies with the electron density at the acyl carbons and with the relative stabilities of the corresponding acylium ions. Thus the ability of the acyl substituent to stabilize a positive charge on the carbonyl carbon seemed to be important. To test this hypothesis further, we have prepared *p*-acetylphenyl- (**1**), phenyl- (**2**), and *p*-methoxyphenyl (**3**) 3-guaiazulenecarboxylates and examined their thermolytic behavior. Differences in the products from **1** to **3** due to steric factors would be small.

## Results and Discussion

Esters **1**—**3** were prepared by the reaction of S-guaiazulene (**4**) with phosgene to form S-guaiazulene-3-carbonyl chloride, and the latter was treated with the corresponding phenol.[6)] Compounds **1** and **3** are new and were characterized by their UV, IR, NMR and mass spectra. During the isolation of **3** a crystalline by-product was obtained which was shown to be bis(*p*-methoxyphenyl) carbonate. This indicates that the acid chloride product contained phosgene in this case.

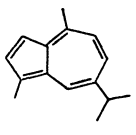


**1**: R=Ac
**2**: R=H
**3**: R=OMe

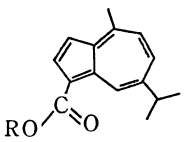
Thermolysis of the esters was carried out at 250 °C for one hour. As anticipated, differences in the products formed or in their relative amounts were found. Only elimination of the carbonyl moiety to give **4** was observed with the *p*-acetylphenyl ester (**1**). In sharp contrast, the phenyl (**2**) and *p*-methoxyphenyl (**3**) esters formed four azulenic products resulting from (i) loss of the ester group (**4**) (ii) migration of the ester group to C-1 with concomitant loss of the 1-methyl group (**5** or **6**), (iii) interchange of the 1-methyl and 3-ester group (**7** or **8**), and (iv) cyclization of the 4-methyl group (**9**). The NMR spectra of compounds **5**—**8** exhibited a characteristic marked low field chemical shift of 8-hydrogen due to the peri ester function. The structures of **5**—**8** were confirmed by conversion to the corresponding known methyl esters (**10** and **11**) by the method of Reimer and Downes.[7)] The yield data are summarized in Table 1. There is a definite correlation between the yields of rearranged products and the ability of the aryl portion of the ester function to supply electrons to the carbonyl carbon. This supports the hypothesis of an ionic mechanism wherein an increase in positive charge on the carbonyl carbon is involved. In that the loss of the ester group to form **4** demonstrates the presence

TABLE 1. YIELDS OF THERMOLYSIS PRODUCTS

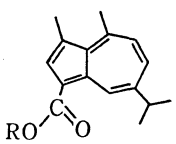
| Ester | Products (%) | | | |
|---|---|---|---|---|
| **1** | **4**(29.3) | | | |
| **2** | **4**(11.8) | **5**(3.4) | **7**(1.6) | **9**(1.4) |
| **3** | **4** (5.1) | **6**(3.3) | **8**(6.1) | **9**(5.6) |



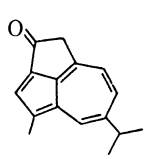
**4**



**5**: R=$C_6H_5$
**6**: R=*p*-$MeOC_6H_5$
**10**: R=Me

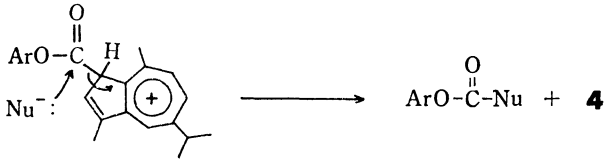


**7**: R=$C_6H_5$
**8**: R=*p*-$MeOC_6H_5$
**11**: R=Me



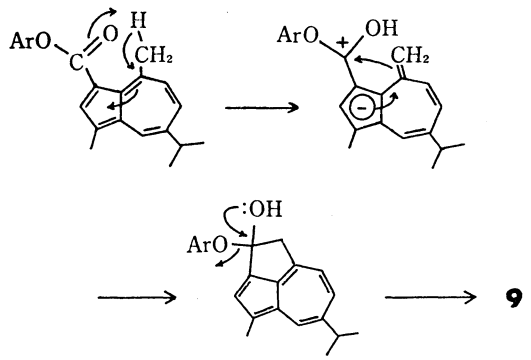
**9**

of a source of protons (perhaps in a decomposition product), reversible electrophilic substitution processes provide the simplest explanation for these reactions. The intermediacy of pi-complexes[8] can explain the formation of the rearrangement products. It is to be noted that all of the products have less steric hindrance than the starting esters and this is presumably the principal driving force. Of interest is the inverse correlation of the yields of **4** with those of the rearranged products. A possible explanation is that **4** is formed, for the most part, directly from the conjugate acid (**12**) through reaction with a nucleophile (*e.g.* the anion of the proton acid). The stability of **12** in terms of the tendency of the ester function to dissociate as a positive ion, or migrate *via* a pi-complex would decrease with the electron-donating ability of the ester aryl group, in agreement with the results obtained.




**12**

The formation of **9** is explicable in terms of the juxta-position of the acidic 4-methyl group[9] and a basic carbonyl oxygen. A simplified scheme is shown. The decreased oxygen basicity in **1** would correlate with the absence of **9** as a product in this case.




## Experimental

NMR spectra were taken in $CDCl_3$, unless otherwise specified, on a JEOL MH-100 spectrometer (100 MHz) with TMS as internal standard. Mass spectra (MS) were obtained at 70 eV with a Hitachi-RMS-4 instrument. UV spectra were recorded in cyclohexane on a Hitachi 624 Digital Spectrophotometer with a Hitachi 056 Recorder, and IR spectra (liquids as films; solids as KBr disks) on a Hitachi EPI-S2 spectrophotometer. Mps are uncorrected. Kanto-Kagaku silica gel was used for chromatography unless otherwise specified. GLC was carried out on a Shimadzu GC-3AH instrument.

*p-Acetylphenyl 3-Guaiazulenecarboxylate (**1**), Phenyl 3-Guaiazulenecarboxylate (**2**), and p-Methoxyphenyl 3-Guaiazulenecarboxylate (**3**)* were prepared from guaiazulene according to the method of Treibs[6] in 44.3%, 31.4% and 29.8% crude (one spot on TLC) and 31.2%, 6.65% and 22.4% pure overall yields, respectively. Ester **1** was obtained from hexane as reddish-purple needles, mp 117.2—117.7 °C. TLC (benzene) $R_f$ 0.11. $\lambda_{max}$: 251 (log $\varepsilon$ 4.70), 305 (4.70), 318 (4.69), 388 (4.36), 524 (sh $\varepsilon$ 612), 562 (755), 613 (sh 570), 673 (sh 175). IR: 1668 and 1702 $cm^{-1}$. NMR ($\delta$): 1.38 (6H, d, $J$= 7.0 Hz $(CH_3)_2CH$), 2.57 (6H, s, 1-$CH_3$ and $COCH_3$), 3.02 (3H, s, 4-$CH_3$), 3.12 (1H, m, $J$=7.0 Hz, $(CH_3)_2CH$), 7.27 (2H, d, $J$=8.0 Hz, 9-H and 12-H), 7.30 (1H, d, $J$=11 Hz, 5-H), 7.5 (1H, dd, $J$=11.0 and 2.0 Hz, 6-H), 7.95 (2H, d, $J$=8.0 Hz, 10-H and 11-H), 8.11 (1H, s, 2-H), and 8.20 (1H, d, $J$=2.0 Hz, 8-H). MS: *m/e* 360 ($M^+$ for $C_{24}H_{24}O_3$) and 225 ($M^+-CH_3COC_6H_5O$).

Ester **2** was isolated as violet plates from ethanol mp 62—63 °C (lit,[6] 69—70.5 °C). TLC (benzene) $R_f$ 0.38. $\lambda_{max}$: 249 (log $\varepsilon$ 4.40), 304.5 (4.53), 315 (sh 4.46), 386 (4.02), 482 (sh $\varepsilon$ 190), 567 (527), and 650 (sh 404). IR: 1718 $cm^{-1}$. NMR ($\delta$): 1.39 (6H, d, $J$=7.5 Hz, $(CH_3)_2CH$), 2.66 (3H, s, 1-$CH_3$), 3.12 (3H, s, 4-$CH_3$), 3.18 (1H, m, $J$=7.5 Hz, $(CH_3)_2CH$), 7.36 —7.56 (6H, 4 lines, $C_6H_5$ and 5-H), 7.68 (1H, dd, 6-H, $J$=2.0 and 10.9 Hz), 8.35 (1H, s, 2-H) and 8.42 (1H, d, $J$=2.0 Hz, 8-H). MS: *m/e* 318 ($M^+$ for $C_{22}H_{22}O_2$) and 225 ($M^+-C_6H_5O$). NMR ($\delta$) ($CF_3COOH$) of the conjugate acid: 1.60 (6H, d, $J$=6.8 Hz, $(CH_3)_2CH$), 2.55 (3H, m, $J$=1.4 and 2.7 Hz, 1-$CH_3$), 3.17 (3H, s, 4-$CH_3$), 3.57 (1H, m, $J$=6.8 Hz, $(CH_3)_2CH$), 5.48 (1H, m, 3-H), 6.8—7.6 (6H, $C_6H_5$ and 2-H), 8.71 (2H, s, 5-H and 6-H), and 8.75 (1H, s, 8-H) showing ring protonation at C-3.

Ester **3** separated from hexane as violet crystals, mp 96.8—97.3 °C. TLC (benzene) $R_f$ 0.29. $\lambda_{max}$: 247 (log $\varepsilon$ 4.85), 303 (4.89), 315 (sh 4.54), 387 (4.22), 531 (sh $\varepsilon$ 586), 569 (728), 621 (sh 549), 684 (sh 193). IR: 1110 (C–O–C), 1170 (C–O–C) and 1703 $cm^{-1}$ (C=O). NMR ($\delta$): 1.35 (6H, d, $J$=7.0 Hz, $(CH_3)_2CH$), 2.57 (3H, s, 1-$CH_3$), 3.02 (3H, s, 4-$CH_3$), 3.08 (1H, m, $J$=7.0 Hz, $(CH_3)_2CH$), 3.75 (3H, s, $OCH_3$), 6.88 (2H, d, $J$=8.9 Hz, 10-H and 11-H), 7.10 (2H, d, $J$=8.9 Hz, 9-H and 12-H), 7.25 (1H, d, $J$=10.9 Hz, 5-H), 7.48 (1H, dd, $J$=10.9 and 2.1 Hz, 6-H), 8.11 (1H, s, 2-H) and 8.20 (1H, d, $J$=2.1 Hz, 8-H). MS: *m/e* 348 ($M^+$ for $C_{23}H_{24}O_3$) and 2.25 ($M^+-CH_3OC_6H_4O$).

In the preparation of **3**, the treatment of the crude ester product with petroleum ether — 1% benzene afforded an insoluble crystalline product which was chromatographed on silica gel (benzene) and then recrystallized from methanol. The colorless needles, mp 98.1 °C, TLC (benzene) $R_f$ 0.51 (spot developed with $HNO_3$–$H_2SO_4$), had spectral properties consistent with those expected for bis(*p*-methoxyphenyl) carbonate. IR: 1234 (C–O), 1763 (C=O) and 2830 $cm^{-1}$ (ether C–H). NMR ($\delta$): 3.77 (6H, s, $OCH_3$), 6.84 and 7.11 (8H, $A_2B_2$, $J_{AB}$=9.0 Hz, $C_6H_4$).

*Thermolysis of Esters **1**, **2** and **3**.*[10] The general procedure was to heat the ester (deoxygenated under high vacuum) sealed in a glass tube under nitrogen at 250 °C for 1 h. The treatment of the glass tube with acid or alkali gave no notable effect on thermolysis. The material was chromatographed on silica gel using a Toyo Kagaku Sangyo SF-160K automatic fraction collector. Benzene eluted S-guaiazulene (**4**) in the first fraction, then in the case of **1**, unchanged starting material. In the cases of **2** and **3**, a mixture of isomerized products, phenyl or *p*-methoxyphenyl 4-methyl-7-isopropyl-1-azulenecarboxylate (**5** or **6**) and the corresponding 3,4-dimethyl-7-isopropyl-1-azulenecarboxylate (**7** or **8**) was eluted after **4**, then unchanged starting material and, finally, benzene–ether (10 : 1) eluted 5-isopropyl-7-methyl-1,2-dihydrocyclopenta[*c*,*d*]azulen-1-one (**9**). Some tary material was obtained as the last fraction in the cases of **1** and **2**. The purity of the starting ester and of each product was checked by GLC

(SE 30 on Chromosorb W at 170—270 °C). The properties ($R_f$ on TLC, IR, NMR and MS) of **4** were shown to be the same as those of an authentic sample. The complete separation of **5** and **7** and of **6** and **8** were very difficult and the yields reported include small correction factors based on GLC and NMR peak ratios.

From 151.8 mg of **1** were obtained 44.5 mg (29.3%) of **4** and 17.7 mg (11.7%) of tary material.

From 1.169 g of **2** were isolated 137.5 mg (11.8%) of **4**, 51.2 mg (4.4%) of unchanged **2**, and 636.8 mg (54.5%) of tar. The mixture of ester products was separated by chromatography on Amberlite IRC-50 (CG-50 Type 2) with 80% ethanol to give 39.6 mg (3.4%) of **5** and 18.8 mg (1.6%) of **7**. Ester **5** was obtained as a reddish violet oil. TLC (benzene) $R_f$ 0.51. $\lambda_{max}$: 241 (log $\varepsilon$ 4.43), 298 (4.62), 304 (4.64), 336.5 (3.72), 344 (3.75), 364 (3.99), 377 (4.09), 510 (sh $\varepsilon$ 677), 532 (827), 570 (749) and 623 (300). IR: 1696 $cm^{-1}$ (C=O). NMR ($\delta$): 1.38 (6H, d, $J$=7.4 Hz, $(C\underline{H}_3)_2CH$), 2.93 (3H, s, 4-$CH_3$), 3.19 (1H, m, $J$=7.4 Hz, $(CH_3)_2C\underline{H}$), 7.23—7.51 (7H, m, $C_6H_5$, 3-H and 5-H), 7.70 (1H, dd, $J$=10.7 and 2.2 Hz, 6-H), 8.46 (1H, d, $J$=4.6 Hz, 2-H), and 9.84 (1H, d, $J$=2.2 Hz, 8-H). MS: *m/e* 304 ($M^+$ for $C_{21}H_{20}O_2$) and 78 ($C_6H_6^+$). Ester **7** was obtained as a violet oil. TLC (benzene) $R_f$ 0.51. $\lambda_{max}$: 248 (log $\varepsilon$ 4.48), 302 (4.64), 309 (4.66), 314 (sh 4.57), 377 (4.05), 389 (4.14), 562 ($\varepsilon$ 887), 602 (sh 730) and 665 (258). IR: 1690 $cm^{-1}$ (C=O). NMR ($\delta$): 1.33 (6H, d, $J$=7.5 Hz, $(C\underline{H}_3)_2CH$), 2.82 (3H, s, 3-$CH_3$), 3.06 (3H, s, 4-$CH_3$), 3.15 (1H, m, $J$=7.5 Hz, $(CH_3)_2C\underline{H}$), 7.12—7.32 (6H, m, $C_6H_5$ and 5-H), 7.47 (1H, dd, $J$=10.7 and 2.0 Hz, 6-H), 8.21 (1H, s, 2-H), and 9.72 (1H, d, $J$=2.0 Hz, 8-H). MS: *m/e* 318 ($M^+$ for $C_{22}H_{22}O_2$), 225 ($M^+-C_6H_5O$) and 211 ($M^+-C_6H_5OCH_2$). Ketone **9** (16.6 mg, 1.4%) crystallized from hexane as dark violet needles, mp 99—100 °C. TLC (10 : 1 benzene–ether) $R_f$ 0.13. $\lambda_{max}$: 235 (log $\varepsilon$ 4.44), 242 (4.44), 258 (4.26), 268 (4.35), 300 (sh 4.36), 304 (4.47), 312 (4.51), 318 (4.62), 350 (sh 3.86), 362 (3.98), 375 (sh 3.96), 381 (4.03), 524 (sh $\varepsilon$ 425), 544 (sh 538), 559 (659), 584 (616), 609 (692), 640 (sh 316) and 674 (324). IR: 1651 $cm^{-1}$ (C=O). NMR ($\delta$): 1.42 (6H, d, $J$=7.5 Hz, $(C\underline{H}_3)_2CH$), 2.65 (3H, s, 7-$CH_3$), 3.22 (1H, m, $J$=7.5 Hz, $(CH_3)_2C\underline{H}$), 4.04 (2H, s, $CH_2$), 7.32 (1H, d, $J$=12.8 Hz, 3-H), 7.68 (1H, s, 8-H), 7.82 (1H, dd, $J$=12.8 and 1.7 Hz, 4-H) and 8.29 (1H, d, $J$=1.7 Hz, 6-H). MS: *m/e* 224 ($M^+$ for $C_{16}H_{16}O$), 209 ($M^+-CH_3$), and 165 ($M^+-C_3H_7O$).

From 814.0 mg of **3** were obtained 41.5 mg (5.1%) of **4** and 437.3 mg (53.7%) of unchanged **3**. The mixture of ester products was treated as described above for the isolation of **5** and **7** and gave 26.9 mg (3.3%) of **6** and 49.8 mg (6.1%) of **8**. Ester **6** was obtained as a red oil. TLC (benzene) $R_f$ 0.32. $\lambda_{max}$: 241 (log $\varepsilon$ 4.45), 299 (4.59), 304 (4.61), 309 (sh 4.51), 364 (3.94), 377 (4.03), 513 (sh $\varepsilon$ 738), 535 (888), 569 (715) and 623 (301). IR: 1692 (C=O) and 2830 $cm^{-1}$ (O–$CH_3$). NMR ($\delta$): 1.35 (6H, d, $J$=6.6 Hz, $(C\underline{H}_3)_2CH$), 2.85 (3H, s, 4-$CH_3$), 3.10 (1H, m, $J$=6.6 Hz, $(CH_3)_2C\underline{H}$), 3.72 (3H, s, $OCH_3$), 6.78 (2H, d, $J$=9.3 Hz, H-10 and H-11), 7.01 (2H, d, $J$=9.3, H-9 and H-12), 7.08 (1H, d, $J$=4.3 Hz, 3-H), 7.22 (1H, d, $J$=10.7 Hz, 5-H), 7.48 (1H, dd, $J$=10.7 and 2.2 Hz, 6-H), 8.24 (1H, d, $J$=4.3 Hz, 2-H) and 9.60 (1H, d, $J$=2.2 Hz, 8-H). MS: *m/e* 334 ($M^+$ for $C_{22}H_{22}O_3$) and ($M^+-CH_3OC_6H_4O$). Ester **8** crystallized from hexane as dark violet crystals, mp 91—92 °C. TLC (benzene) $R_f$ 0.32. $\lambda_{max}$: 249 (log $\varepsilon$ 4.57), 289 (sh 4.53), 300 (4.71), 308 (4.73), 314 (sh 4.66), 373 (4.14), 388 (4.21), 526 (sh $\varepsilon$ 760), 562 (990), 604 (sh 826) and 666 (301). IR: 1700 $cm^{-1}$. NMR ($\delta$): 1.35 (6H, d, $J$=7.2 Hz, $(C\underline{H}_3)_2CH$), 2.83 (3H, s, 3-$CH_3$), 3.05 (3H, s, 4-$CH_3$), 3.08 (1H, m, $J$=7.2 Hz, $(CH_3)_2C\underline{H}$), 3.80 (3H, s, $OCH_3$), 6.94 (2H, d, $J$=9.6 Hz, H-10 and H-11), 7.16 (2H, d, $J$=9.6 Hz, H-9 and H-12), 7.19 (1H, d, $J$=10.5 Hz, 5-H), 7.48 (1H, dd, $J$=10.5 and 2.0 Hz, 6-H), 8.23 (1H, s, 2-H) and 9.76 (1H, d, $J$=2.0 Hz, 8-H). MS: *m/e* 348 ($M^+$ for $C_{23}H_{24}O_3$) and 225 ($M^+-CH_3OC_6H_4O$). The yield of ketone **9** was 45.8 mg (5.6%).

*Methyl 4-Methyl-7-isopropyl-1-azulenecarboxylate (**10**).* *A. From **5**.* A solution of 20.98 mg of **5** in an excess (0.7 ml) of 0.03 M potassium methoxide in methanol was shaken in a sealed tube for 20 h. The mixture was then diluted with water (30 ml) and extracted with ether (3×10 ml). Chromatography of the concentrate from the ether extract on silica gel (benzene) separated 12.60 mg (75.4%) of **10** identical (UV, IR and NMR) with an authentic specimen.[11]

*B. From **7**.* The procedure given in *A* afforded 8.97 mg (85.4%) of **10**, identical (IR, NMR) with that from *A*, from 14.43 mg of **7**.

*Methyl 3,4-Dimethyl-7-isopropyl-1-azulenecarboxylate (**11**).* A. *From **6**.* In the manner described for the preparation of **10**, 4.42 mg of **6** was converted to 2.05 mg (57.6%) of **11** identical (UV, Vis, TLC) with an authentic specimen.[4]

*B. From **8**.* The procedure indicated in *A* gave from 5.96 mg of **8** a yield of 3.98 mg (90.9 %) of **11** identical with that from *A*.

## References

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